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SUPPLEMENT 5

27th Annual Scientific Meeting of The Hong Kong Neurological Society

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List of Speakers

Name	Affiliation
Prof Andrew Chan	Ruhr-University Bochum, Germany
Dr Larry Chan	Alice Ho Miu Ling Nethersole Hospital, Hong Kong SAR
Dr Carlin Chang	Queen Mary Hospital, Hong Kong SAR
Prof Chern-En Chiang	Taipei Veterans General Hospital and National Yang-Ming University, Taiwan
Ms Wai-ka Choy	Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR
Dr Jonathan Chu	Princess Margaret Hospital, Hong Kong SAR
Prof Liying Cui	Peking Union Medical College Hospital, China
Dr Andrew Evans	The Royal Melbourne Hospital, Australia
Dr Florence SY Fan	Prince of Wales Hospital, Hong Kong SAR
Dr Jason KY Fong	Hong Kong Epilepsy Society, Hong Kong SAR
Prof Marco Franceschini	IRCCS San Raffaele, Pisana – Rome, Italy
Prof Toshiyuki Fujiwara	Tokai University School of Medicine, Japan
Prof Nobutaka Hattori	Juntendo University, Japan
Dr Wai-ki Ip	Queen Mary Hospital, Hong Kong SAR
Dr Moamina Ismail	Queen Elizabeth Hospital, Hong Kong SAR
Prof Ryuji Kaji	University of Tokushima Graduate School of Medicine, Japan
Dr Hon-hang Kwan	Princess Margaret Hospital, Hong Kong SAR
Ms Trase CM Kwok	Tseung Kwan O Hospital, Hong Kong SAR
Dr Jacky Lee	Queen Mary Hospital, Hong Kong SAR
Dr Howan Leung	Prince of Wales Hospital, Hong Kong SAR
Prof Wei-ping Liao	The Second Affiliated Hospital of Guangzhou Medical University; Key Laboratory of Neurogenetics and Channelopathies of Guangdong Province and the Ministry of Education of China, China
Prof Bai Lui	Tsinghua University Medical School, China
Prof Vincent Mok	Prince of Wales Hospital, Hong Kong SAR
Dr Ping-wing Ng	United Christian Hospital, Hong Kong SAR
Dr Yee-wah Ng	Kowloon Hospital, Hong Kong SAR
Dr Sven Schippling	University Medical Center Zurich, Switzerland
Prof Lin Shi	Prince of Wales Hospital, Hong Kong SAR
Dr Yannie Soo	Prince of Wales Hospital, Hong Kong SAR
Prof Angela Vincent	University of Oxford, United Kingdom
Prof Matthew Walker	UCL Institute of Neurology, UCL, London and National Hospital for Neurology and Neurosurgery, United Kingdom
Dr Wa-tai Wong	Princess Margaret Hospital, Hong Kong SAR

SCIENTIFIC PROGRAMME

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

1 November 2014, Saturday

08:30 – 08:45	Registration	Poster Room
08:45 – 09:45	**FREE PAPER PRESENTATION** *Chairpersons: Thomas Leung, Paul Chang* *Judges: SH Ng, David Chin*	**POSTER PRESENTATION**
09:45 – 10:00	Coffee Break	
10:00 – 11:25	**DISSERTATION HIGHLIGHTS** *Chairpersons: Thomas Leung, Paul Chang* *Judges: SH Ng, David Chin*	
11:25 – 12:05	**MERCK SERONO SYMPOSIUM ON MULTIPLE SCLEROSIS** *Chairperson: Winnie Wong* **Therapy for Multiple Sclerosis: the Evidence, the News and the Future** *Andrew Chan*	
12:05 – 13:05	**NOVARTIS LUNCH SYMPOSIUM** *Chairperson: Wing-keung Cheng* **Brain Volume Loss in Multiple Sclerosis: Implications on Clinical Outcomes** *Sven Schippling*	
13:05 – 13:30	**OPENING CEREMONY** Guest of Honour: *Prof Gabriel Leung, GBS, JP, Dean, Li Ka Shing Faculty of Medicine, the University of Hong Kong* Opening Remarks: *Dr Jonas HM Yeung, President of the Hong Kong Neurological Society*	
13:30 – 15:00	**NEUROPHYSIOLOGY SYMPOSIUM** *Chairpersons: Leonard Li, YW Chan* **Serial Electrophysiological Study of Guillain-Barré Syndrome** *Liying Cui* **Physiology and Clinical Diagnosis of Amyotrophic Lateral Sclerosis and Related Diseases** *Ryuji Kaji* **Electroencephalography in Hong Kong: Teaching, Service, and Research** *Howan Leung*	
15:00 – 15:30	Coffee Break	
15:30 – 17:00	**NEURO-IMMUNOLOGY SYMPOSIUM** *Chairpersons: SH Ng, KK Lau* **The Role of Immunology in Neuromuscular Junction Diseases** *Angela Vincent* **Multiple Sclerosis Treatment Strategy for Long-term Clinical Outcome** *Sven Schippling* **Testing for Neutralising Antibodies to Interferon-beta in Patients with Multiple Sclerosis** *WK Ip*	
18:00	Faculty Dinner (by invitation only)	

2 November 2014, Sunday

08:30 – 09:00	Registration	Poster Room
09:00 – 10:30	**BOEHRINGER INGELHEIM STROKE AND NEURO-REHABILITATION SYMPOSIUM** *Chairpersons: CM Cheung, Patrick Li* **Full Analyses of New Oral Anticoagulants in Atrial Fibrillation: Global Versus Asian** *Chern-En Chiang* **Action-observation in Upper Limb Stroke Rehabilitation in Sub-acute Phase** *Marco Franceschini* **Hybrid Assistive Neuromuscular Dynamic Stimulation (HANDS) Therapy: New Therapeutic Strategy for Hemiparetic Upper Extremity After Stroke** *Toshiyuki Fujiwara*	**POSTER PRESENTATION**
10:30 – 10:45	Coffee Break / Poster Viewing Session *Judges: Raymond Chan, Mona Tse*	
10:45 – 12:15	**DEMENTIA SYMPOSIUM** *Chairpersons: Vincent Mok, CK Wong* **Challenges and Opportunities in Drug Discovery for Neurodegenerative Diseases** *Bai Lu* **Advanced Magnetic Resonance Imaging Techniques in the Evaluation of Preclinical Alzheimer's Disease** *Lin Shi* **Cerebrovascular Disease, Amyloid Plaques, and Cognitive Impairment** *Vincent Mok*	

(Cont'd on p.8)

12:15 – 13:30	**BAYER LUNCH SYMPOSIUM** *Chairperson: TH Tsoi* **Stroke Prevention in Asian Atrial Fibrillation Patients** *Ping-wing Ng*	Poster Room **POSTER PRESENTATION**
13:30 – 15:00	**EPILEPSY SYMPOSIUM** *Chairpersons: Guardian Fong, Eric Chan* **Diagnosis and Management of Non-convulsive Status Epilepticus** *Jason KY Fong* **Gene Therapy in the Treatment of Epilepsy** *Matthew Walker* **Channelopathy and Pharmacoresistance** *Wei-ping Liao*	
15:00 – 15:15	Coffee Break	
15:15 – 16:45	**MOVEMENT DISORDERS SYMPOSIUM** *Chairpersons: Nelson Cheung, KL Tsang* **The Basic Science Underlying Dopamine Dysregulation Syndrome and Impulse Control Disorders in Parkinson's Disease and the Implications of These Phenomena on the Treatment** *Andrew Evans* **The Use of Parkinson's KinetiGraph Technology on Parkinson's Disease's Treatment** *Andrew Evans* **Pharmacological Treatments of Parkinson's Disease: the Concept of Once-daily Dopamine Agonist Therapy** *Nobutaka Hattori*	
16:45 – 17:00	Closing Remarks & Award Presentation	

FP 1

Integrated Parkinson's Disease Service Part I: Alteration of Postural Sensory Conflict in Dynamic Balance Control Among Patients with Idiopathic Parkinson's Disease

Trase CM Kwok[1], KF Hui[2], Colin HT Lui[2], PY Lau[1], YW Cheung[1], TK Au[1]
[1] Physiotherapy Department, Tseung Kwan O Hospital, Hong Kong SAR
[2] Department of Medicine, Tseung Kwan O Hospital, Hong Kong SAR

Background: Idiopathic Parkinson's disease (iPD) is known to affect postural control, especially in situation needing a change in balance strategy or when a concurrent task is simultaneously performed. In clinical practice, evaluation of postural control is based on the neurological examination, including Romberg's test, examination of gait, and performance of pull test as part of the Unified Parkinson's Disease Rating Scale (UPDRS). There are few studies assessing quantities of postural control parameter in clinical routine use in fallers and non-fallers of iPD patients.

Objectives: (1) To determine the posturographic parameters among the fallers and non-fallers of iPD patients by means of computerised dynamic posturography using Sensory Organization Test (SOT); and (2) to identify the determining factors which contribute to postural instability that help in prediction of fall risks. These will contribute to balance and mobility training and fall prevention of PD rehabilitation in clinical practice.

Methods: A prospective study of 33 iPD patients in Integrated Parkinson's Disease Service was conducted. The dynamic postural control of 17 fallers and 16 non-fallers was studied by SOT during their 'on' medication period, using Neurocom Smart Balance Master (Clackamas [OR], US). This computerised dynamic posturography system allows independent evaluation of the contributions of vestibular, visual, and proprioceptive inputs to the maintenance of dynamic balance.[1]

Results: Faller group performed significantly worse than the non-faller group under SOT conditions 5 and 6. The average balance score was poorer in the faller group ($P<0.01$). The somatosensory input and the vestibular input were predominantly impaired and contributed to fall in iPD patients. The PD progression stage, motor control, number of non-motor symptoms, and health condition were more deteriorated in the faller group ($P<0.05$). The impaired postural instability measured by average balance score in SOT was significantly correlated to reduced motor control (UPDRS motor), number of non-motor symptoms, disease progression stage (Hoehn & Yahr stages), number of chronic diseases that patients needed medication intervention, vestibular and visual input ($P<0.01$; motor score UPDRS $r = -0.526$, non-motor symptoms $r = -0.434$, disease progression stage $r = -0.554$, number of chronic diseases $r = -0.418$, vestibular input $r = 0.776$, and visual input $r = 0.619$).

Conclusion: Balance impairment is seriously affected in iPD patients at various disease progression stages. Somatosensory and vestibular input dysfunction probably plays a role in their instability and contributing to falls. As iPD is a central nervous system disorder, such deficiency suggests a dysfunction in central processing rather than a peripheral lesion. The postural stability control is related to numerous factors in fallers, like somatosensory, vestibular input, disease progression stage, motor score in UPDRS, and non-motor symptoms. Therefore, a battery of tests including SOT is highly recommended to assess the fall risk objectively quantified in routine clinical situation. They are reliable parameters for monitoring balance progression in clinical fall management.

Reference

1. Rossi M, Soto A, Santos S, Sesar A, Labella T. A prospective study of alterations in balance among patients with Parkinson's Disease. Protocol of the postural evaluation. Eur Neurol 2009;61:171-6.

FP 2

Integrated Parkinson's Disease Service Part II: Efficacy of Integrated Care Model on Disease Management, Functions Regained, and Fall Management

Trase CM Kwok[1], KF Hui[2], Colin HT Lui[2], PY Lau[1], SA Lai[3], YW Cheung[1], TK Au[1]
[1] Physiotherapy Department, Tseung Kwan O Hospital, Hong Kong SAR
[2] Department of Medicine, Tseung Kwan O Hospital, Hong Kong SAR
[3] Nursing Service, Department of Medicine, Tseung Kwan O Hospital, Hong Kong SAR

Background: Integrated Parkinson's Disease Service (IPDS) is a collaboration work between Department of Medicine, Physiotherapy Department, and Nursing Service of Department of Medicine. Inside, multidisciplinary team approach is adopted. Interventions included (1) holistic one-stop, fast-track, multidisciplinary comprehensive assessment on health, disease condition, and physical functions on the same platform; (2) providing risk stratifications for triage and efficient access to different professions for comprehensive service including deep brain stimulation for further care; (3) optimising clients' medical control, physical and motor functions, and well-being with participation in specific exercise programme in Physiotherapy Department.

Objectives: To verify the effectiveness of IPDS on disease management, physical functions, and postural sensory conflict in dynamic balance control for fall management.

Methods: IPDS in Day Medical Center for idiopathic Parkinson's disease (iPD) care enhancement was established. A total of 34 participants with iPD that ranged from stage I to stage III on the Hoehn & Yahr (H&Y) scale were completed at 6 months' follow-up. They all received medical management from experienced neurologists, health care management advice from nurses, and engaged in 'Parki-Fit Walk & Balance Program' in Physiotherapy Department. The medical management was focused on motor and non-motor symptom control, motor fluctuation, complications, and all other health care. The compromised workflow and structured 'Parki-Fit Walk & Balance Program' were adopted and implemented. Disease progression, motor and non-motor control, physical fitness (included physical endurance and comfort gait speed), and dynamic postural stability were assessed in pre- versus post-methodology. The dynamic postural control of 17 fallers and 17 non-fallers were studied by Sensory Organization Test (SOT), using Neurocom Smart Balance Master (Clackamas [OR], US). All assessments were performed during patients' 'on' medication period.

Results: Univariate analyses showed that both fallers and non-fallers iPD patients improved their motor control, non-motor symptoms, physical fitness, ambulatory functions, and postural stability control after the IPDS. The amounts of net increase in functions, motor control, and postural stability control were the same in both groups. In summary, the Unified Parkinson's Disease Rating Scale motor score improved by 20.8%, non-motor score improved by 30.8%, physical fitness as measured by a distance of 6-minute walk improved by 26.7%, ambulatory like comfort gait speed improved by 31.2%, overall balance score in SOT improved by 27%, and vestibular input in postural stability control improved by 86% ($P<0.001$). The total number of fall episodes significantly dropped by 63%, from 46 episodes to 17 episodes after the IPDS intervention. The results will be illustrated in the graphs and tables.

Conclusion: The multidisciplinary IPDS served the purpose of better health and disease management of iPD, as well as geared towards better functions and fall management. It is highly recommended to conduct further studies to determine its long-term effect on patient care outcomes.

FP 3

Treatment of Autoimmune Neurological Disorders with Therapeutic Plasma Exchange: a Local Regional Hospital Experience

WK Choy, WH Cheng, R Li, CM Cheung, SY Liu, HY Cho, BY Lo
Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

Background: Therapeutic plasma exchange (TPE) is a well-established treatment for many autoimmune neurological disorders. Its advantage lies in its rapid onset of action, by direct removal of pathogenic auto-antibodies. However, access to this treatment modality may be difficult. Close collaboration between the Neurology Team and Haematology Nurse Specialist in Pamela Youde Nethersole Eastern Hospital (PYNEH) has made TPE an accessible treatment option in our centre.
Methods: All patients with neurological disorders who required TPE between October 2011 and August 2014 in PYNEH were retrospectively reviewed. Data were collected on demographics, methodology, indication, and treatment details of TPE; complication and mortality rate; and functional outcome measured by changes in modified Rankin Scale (mRS) 3 months after TPE compared with premorbid.
Results: Overall, 22 subjects were identified. Their mean age was 57 years, with a female preponderance (59.1%). TPE was performed by the Spectra Optia or Haemonetics cell separator. Indications for TPE included Guillain-Barré syndrome (n=5), myasthenia gravis (n=4), autoimmune encephalitis (n=5), neuromyelitis optica (n=5), and myelitis of other causes (n=3). Twenty patients received intravenous immunoglobulin or steroid therapy prior to TPE; two received TPE as first-line treatment. A total of 97 exchanges were performed, with a mean of four sessions per patient, and a mean processed plasma volume of 3677 mL per cycle. TPE was well tolerated. Hypotension and hypocalcaemia were common, but responded well to replacement therapy. No complications or mortality arose from TPE. Four patients were still in rehabilitation at the time of writing. Of the 18 remaining subjects, 13 (72.2%) had mRS change of <2.
Conclusion: TPE is an effective and safe treatment for autoimmune neurology diseases. In view of the increasing awareness and expanding spectrum of autoimmune-related neurological diseases, it is worth to invest in training more nurse specialists who are specialised in therapeutic apheresis to make TPE more easily accessible.

FP 4

HAT Score is a Useful Risk-predicting Tool in Stroke Thrombolysis

HH Kwan, KK Lau, B Sheng, MK Fong, YP Chu, WT Wong
Division of Neurology, Department of Medicine, Princess Margaret Hospital, Hong Kong SAR

Background: Haemorrhage After Thrombolysis (HAT) score has been used to predict the risk of symptomatic intracranial haemorrhage (SICH) in ischaemic stroke patients receiving intravenous tissue plasminogen activator (t-PA). This study aimed to evaluate its value in the Chinese population.
Methods: We reviewed 81 consecutive intravenous stroke thrombolysis treatments in Princess Margaret Hospital and calculated the HAT score (range, 0-5) for each patient using their admission clinical data (pre-treatment NIHSS (National Institutes of Health Stroke Scale), presence of visible hypodensity on initial head computed tomography [CT] scan, history of diabetes mellitus, and baseline serum glucose). The outcomes of interest were SICH as defined in the HAT original validation cohort (any CT-documented ICH within 72 hours from stroke onset that was temporally related to clinical deterioration) and the modified Rankin Scale score (mRS) at 3 months.
Results: The percentage of patients who developed SICH after t-PA increased with higher HAT scores. The rate of SICH was 0% (0 point), 0% (1 point), 10% (2 points), and 13% (≥3 points). The score also reasonably predicted good (mRS ≤3) and catastrophic (mRS ≥5) functional outcomes at 3 months. The predicted rates for SICH and poor neurological outcome with HAT score of ≥3 were similar to the published cohorts.
Conclusion: The HAT score is a convenient risk stratification tool for stroke thrombolysis. It could be reliably applied in our patients.

Comparison of Clinical Outcomes between Ischaemic Stroke Patients With or Without Atrial Fibrillation Treated with Intravenous Thrombolysis

FP 5

WT Wong, KK Lau, B Sheng, YP Chu, MK Fong, HH Kwan
Division of Neurology, Department of Medicine, Princess Margaret Hospital, Hong Kong SAR

Background: Atrial fibrillation (AF) is a common cause of ischaemic stroke. It is also believed to be a predictor of poor outcome despite treatment of intravenous thrombolysis. The aim of this study was to evaluate whether the presence of AF would have influence on the clinical outcome of ischaemic stroke patients treated with intravenous thrombolysis.
Methods: This was a single centre retrospective study. Overall, 81 consecutive ischaemic stroke patients treated with intravenous thrombolysis within 4.5 hours from stroke onset were divided into two groups based on the presence or absence of AF. Clinical outcomes of 3-month modified Rankin Scale (mRS), National Institutes of Health Stroke Scale (NIHSS) score at 24-hour post-treatment, and adverse outcome of intracerebral haemorrhage were compared.
Results: Of 81 patients treated with thrombolysis, 37 (46%) had AF. Baseline comparison showed that apart from AF, these patients were significantly older than non-AF patients (mean age, 73 vs 64 years; P=0.003), other parameters including baseline NIHSS and onset-to-needle time were not significantly different between groups. A significantly higher percentage of AF patients had poor 3-month clinical outcome (defined as a mRS of ≥5) than non-AF patients (30% vs 9%; P=0.017). After adjusting the baseline age difference, the association of AF and poor 3-month outcome still showed a trend towards statistical significance (odds ratio=3.18; 95% confidence interval, 0.85-11.89; P=0.085). On the other hand, the 24-hour post-treatment NIHSS, the incidence of intracerebral haemorrhage, and favourable 3-month clinical outcome (defined as a mRS of ≤3) showed no significant difference between the two groups (P=0.233, 0.283, 0.328, respectively).
Conclusion: Ischaemic stroke patients with AF are more likely to have poor 3-month clinical outcome than non-AF patients when treated with intravenous thrombolysis.

Local Experience of TeleStroke Through Out-of-hospital Teleconsultation

FP 6

Yannie Soo, Vincent Ip, CB Leung, C Choi, Anne Chan, Lisa Au, Florence Fan, Alexander Lau, Howan Leung, Vincent Mok, KS Wong, Thomas Leung
Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong SAR

Background: TeleStroke network has been established in several western countries to provide expert opinion for thrombolysis to patients in rural areas. TeleStroke hardware is typically installed in an emergency department or acute stroke unit on stationary workstations or mobile carts. Although a number of studies have reported the feasibility and safety of thrombolysis through TeleStroke, evidence is limited to stroke models with teleconsultations performed within the hospital area where stable internet connection is steadily available for teleconsultation. Up to date, there are no data concerning feasibility and safety of TeleStroke performed outside the hospital area, where WiFi and internet receptions are location-dependent. Here, we report our local experience of TeleStroke through out-of-hospital teleconsultation with mobile devices.
Methods: Due to extreme shortage of neurologists in Hong Kong, on-site neurologists are often not available in hub hospitals during non-working hours. Patients were evaluated through TeleStroke by off-site neurologists with mobile devices outside the hospital area. During May 2012 to September 2014, we evaluated 142 patients for thrombolytic therapy using TeleStroke.
Results: The mean age of the patients was 71.5 ± 14.8 years. A total of 68 patients were given intravenous thrombolysis through TeleStroke. Technical problems during teleconsultation occurred in 17 cases. Comparing the 68 patients by TeleStroke with 64 patients treated by on-site neurologists over the same period, treatment outcome was comparable. Good recovery (defined as 3-month modified Rankin Scale score, 0-1) occurred in 46.0% in TeleStroke-treated patients versus 47.3% treated by on-site neurologists (P=1.000). Symptomatic intracranial haemorrhage occurred in 5.9% in TeleStroke-treated patients versus 4.7% treated by on-site neurologists (P=1.000).
Conclusion: Technical problem is not uncommonly observed during out-of-hospital teleconsultations. Although treatment outcome by TeleStroke is comparable to those treated by on-site neurologists, improvement in TeleStroke hard- and soft-wares are needed to ensure a safe and sustainable TeleStroke service in Hong Kong.

DH 1

Using Clinical and Radiological Parameters to Predict Early Neurological Deterioration in Primary Spontaneous Intracerebral Haemorrhage

YW Ng
Department of Medicine, Kowloon Hospital, Hong Kong SAR

Background: Readily available predictors of early neurological deterioration (END) upon admission can help the clinical decision in managing acute intracerebral haemorrhage (ICH). This study aimed to determine the clinical risk factors for END in primary spontaneous ICH patients who were initially put on conservative treatment.

Methods: Clinical and radiological data were collected from a retrospective cohort of ICH patients who were initially managed conservatively. Only patients admitted within 6 hours of symptom onset were included; END was defined as new onset of neurological deficits and/or deterioration in the presenting neurological deficits within 48 hours from the time of admission. Ultraearly haematoma growth (uHG) was obtained to compare with haematoma volume in predicting END. Potential predictors and factors associated with END ($P<0.05$) were analysed with binary logistic regression.

Results: A total of 104 patients were recruited; 38 (36.5%) patients developed END. Haematoma volume of ≥10 mL, midline shift, and intraventricular extension of haematoma (IVH) were significant predictors of END in the final equation of regression. It was found that uHG was also an independent predictor. It did not appear superior to haematoma volume in predicting END. ROC analysis showed both haematoma volume and uHG could be used for predicting END. Various threshold volumes were explored for each location. For BG ICH, threshold volume of ≥15 mL (sensitivity=0.77, specificity=0.84, and Youden's index=0.61) was preferred. For lobar ICH, threshold volume of ≥25 mL (sensitivity=0.85, specificity=0.67, and Youden's index=0.52) was more appropriate. It was less predictable for thalamic ICH. Only volume of <2 mL was less likely to develop END.

Conclusions: Haematoma volume of ≥10 mL (within 6 hours of symptom onset), midline shift, and IVH were significant predictors of END. Age of ≥80 years was marginally significant. Both baseline haematoma volume and uHG could predict END. uHG did not appear superior to baseline haematoma volume in predicting END. Threshold volume cut-off was different for respective locations. For BG ICH, threshold volume of ≥15 mL was preferred. For lobar ICH, threshold volume of ≥25 mL was more appropriate. It was less predictable for thalamic ICH. Only volume of <2 mL was less likely to develop END.

DH 2

Outcomes in Ischaemic Stroke Patients with Co-existing Intracranial Large-artery Atherosclerotic Stenosis

Larry Chan
Department of Medicine, Alice Ho Miu Ling Nethersole Hospital, Hong Kong SAR

Background: Strokes related to intracranial large-artery stenosis (ILAS) are known to have adverse outcomes, but data on outcomes of asymptomatic ILAS are limited. This study aimed to determine the risk of ischaemic events related to asymptomatic ILAS. The secondary end-points included risk of ischaemic events in any other cerebral vascular territories, mortality, and risk of other vascular events.
Methods: Patients admitted to a local hospital for ischaemic cerebral events from 1 January 2009 to 31 August 2010 were studied. Patients with moderate or severe ILAS unrelated to the index ischaemic event formed the study group, while patients with no or only mild stenosis were the control group. All the patients were followed for 3 years or till their deaths.
Results: A total of 534 adult patients were studied. The mean follow-up time was 33.28 ± 8.31 months. Age ($P<0.0001$) and diabetes mellitus ($P=0.032$) were independent risk factors for the development of ILAS. More patients in the study group had large-vessel disease causing their index ischaemic events while more patients in the control group had small-vessel disease ($P<0.0001$). More patients in the study group received dual antiplatelets upon discharge ($P=0.020$). At 3 years, five (1.9%) patients in the study group and two (0.7%) patients in the control group reached the primary outcome ($P=0.233$). All secondary outcomes did not show any statistically significant difference.
Conclusions: Asymptomatic ILAS in stroke patients does not increase risk of cerebral ischaemic events, mortality, or other vascular events within the subsequent 3 years.

DH 3

Predictors of Outcome in Ischaemic Stroke Patients Receiving Intravenous Thrombolysis

Carlin Chang
Division of Neurology, Department of Medicine, Queen Mary Hospital, Hong Kong SAR

Background: Intravenous (IV) thrombolytic, tissue plasminogen activator (tPA), is widely used and the best available first-line treatment for acute ischaemic stroke when presented within 4.5 hours of stroke onset. This treatment has been found to minimise the area of ischaemic infarct to enable maximum recovery and minimum disability. This study aimed to identify the potential prognostic predictors of stroke outcome in cases that received IV tPA to determine which subset of patients would benefit more from thrombolytic treatment.
Methods: This study included all patients who received IV tPA at the Queen Mary Hospital in Hong Kong for acute ischaemic stroke. Clinical data of 161 subjects were analysed and multiple logistic regression analysis was used to determine which variables could predict the eventual outcome.
Results: The most important predictors of IV tPA outcome were the history of antiplatelet use when tPA was administered (odds ratio [OR]=2.97; confidence interval [CI]=1.13-7.80; $P=0.027$) as well as the final NIHSS score (OR=1.23; CI=1.15-1.32; $P=0.000$). The presence of atrial fibrillation (OR=3.06; CI=1.40-6.67; $P=0.005$) was highly predictive of post-thrombolytic intracerebral haemorrhage while fasting glucose levels (OR=2.26; CI=1.1-4.6; $P=0.026$) was correlated with the presence of symptomatic haemorrhage in post-tPA cases. However, a hyperdense artery sign had a lower risk of symptomatic haemorrhage ($P=0.02$). Advanced age was not a poor indicator of post tPA outcome.
Conclusion: When ischaemic stroke patients are admitted as potential candidates for IV tPA, careful assessment should be made to determine not only whether the patient is eligible for tPA but more importantly who would best benefit from tPA. Based on the results of this study, no specific factor is able to precisely predict the eventual outcome, but particular caution should be made if the patient has been taking an antiplatelet or if the patient has a high serum glucose level in the background of atrial fibrillation as these are associated with a poor tPA outcome (modified Rankin Scale, 4-6).

Late-onset Pompe Disease in Hong Kong

DH 4

Jonathan Chu
Department of Medicine, Princess Margaret Hospital, Hong Kong SAR

Background: Late-onset Pompe disease (LOPD), a rare inherited disease, affects the musculoskeletal system due to reduced α-glucosidase enzyme activity in lysosome. The clinical manifestation is diverse but Chinese population tends to show a more aggressive form of the disease. Enzyme replacement therapy (ERT) was associated with symptom improvement but it varies among individuals. This study aimed at performing an in-depth review of natural history and investigating the treatment response of all LOPD patients in Hong Kong.

Methods: We reviewed all case records and conducted a face-to-face interview to complete a detailed questionnaire regarding clinical manifestation and diagnosis of the disease. We studied the clinical outcomes of ERT by 6-minute walking test (6MWT), forced vital capacity (FVC), MRC (Medical Research Council) sum score, muscle enzymes, and SF-36 questionnaires.

Results: Between 2000 and 2013, 11 patients were identified and one was lost to follow-up. Age of diagnosis ranged from 9 to 44 years. The median age of first symptoms was 20.5 (range, 6-44) years while the median age of first medical attention was 29 (range, 9-44) years. The most common initial complaint was decreased exercise tolerance. One fifth of patients' first complaint was difficulty to get up from lying position and failed to perform sit-up. The mean time from first medical attention to diagnosis was 1.3 years but one patient was diagnosed 8 years later. Half of the patients sought medical attention due to progressive shortness of breath and all of them developed type 2 respiratory failure requiring ventilator support during the first admission. 20% patients were chair-bound and 70% patients required ventilation support. Six patients were put on ERT. They showed a mean absolute increase of 62 m in 6MWT and 8.6% of FVC predicted after 12 months of treatment. The results were sustained at 24 months.

Conclusion: In our population, LOPD patients tend to have an earlier and more aggressive clinical presentation with respiratory insufficiency and they showed a sustained improvement in lung function and walking distance after ERT.

DH 5

An Evaluation of Haemodynamics across Intracranial Steno-occlusive Lesions by Computational Fluid Dynamics

Florence SY Fan
Division of Neurology, Department of Medicine and Therapeutics, Prince of Wales Hospital, Hong Kong SAR

Background: Intracranial atherosclerotic steno-occlusive disease is a major cause of stroke worldwide and portends a high risk of recurrence. Although the degree of arterial stenosis might predict stroke recurrence, it is likely not the sole determining factor for relapse. Notably, collateral flow and the haemodynamics across the culprit lesion may pose a significant impact on stroke risk. Computational fluid dynamics (CFD) is a novel technique developed to solve and analyse the dynamic effects of fluid flow. While cerebral computed tomography angiography (CTA) provides non-invasive anatomical assessment on intracranial atherosclerotic steno-occlusive disease, processing of CTA images by CFD offers functional haemodynamic assessments across the stenosis. We aimed to process CTA images by CFD and explore the correlation between the degree of arterial stenosis and haemodynamic flow status across intracranial atherosclerotic steno-occlusive lesions.
Methods: Patients with stroke and transient ischaemic attack attributed to intracranial atherosclerotic steno-occlusive disease from Acute Stroke Unit, Prince of Wales Hospital, were recruited. All participants received definitive vascular imaging including CTA and digital subtraction angiography (DSA). We first delineated the haemodynamic parameters—including pressure difference, pressure ratio, pressure gradient, shear strain rate ratio (SSR), wall shear stress (WSS) ratio, and velocity ratio—across the stenosed vessels, and then we correlated the degree of arterial stenosis with these haemodynamic parameters.
Results: Among the 53 recruited patients (mean age, 62.9 years; 69.8% males), 45 (85%) had stroke or transient ischaemic attack (TIA) in the carotid circulation. The anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (r_s=0.392, P=0.004), pressure ratio (r_s= –0.429, P=0.001), and pressure gradient (r_s=0.419, P=0.002). There was no significant correlation between the anatomical severity of stenosis with SSR ratio, WSS ratio, and velocity ratio. Among patients with anterior circulation stroke or TIA, the anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (r_s=0.381, P=0.01), pressure ratio (r_s= –0.426, P=0.004), and pressure gradient (r_s=0.407, P=0.005). For patients with posterior circulation stroke or TIA, the anatomical severity of stenosis was strongly correlated with pressure difference (r_s=0.714, P=0.047) and pressure ratio (r_s= –0.714, P=0.047), and very strongly correlated with velocity ratio (r_s=0.833, P=0.01).
Conclusions: The severity of intracranial steno-occlusive disease showed a weak-to-moderate correlation with pressure difference, pressure ratio, and pressure gradient across the culprit lesion. As determination of future stroke risk and treatment based solely on stenotic severity may be inadequate for patients with symptomatic intracranial steno-occlusive disease, our findings may guide further research in the field, specifically, studies on estimating stroke risks and selection of high-risk patients who may benefit from adjunctive treatment like plaque stabilisation or cerebral re-vascularisation. This study also illustrated the potential role of CTA as a non-invasive imaging modality in providing both anatomical and functional assessments for intracranial steno-occlusive disease.

Prognosis and Crisis in Generalised Myasthenia Gravis among Hong Kong Chinese

DH 6

Jacky Lee
Division of Neurology, Department of Medicine, Queen Mary Hospital, Hong Kong SAR

Objectives: To study the clinical features of local generalised myasthenia gravis (gMG) patients, the independent predictors for good long-term outcome and for development of MG crisis, as well as the potential role of cytokines as biomarkers of MG disease activity.
Methods: Local gMG patients managed in Queen Mary Hospital from 1997 to 2012 were retrospectively reviewed. Serum or plasma levels of a number of inflammatory cytokines were measured in a small portion of gMG patients to compare between patients with stable disease and those with MG exacerbation or crisis.
Results: A total of 123 Chinese gMG patients were recruited; 96 (78.0%) patients had good outcome. The use of azathioprine was the only independent predictor of good outcome (odds ratio [OR]=3.57; 95% confidence interval [CI], 1.05-12.10; P=0.042). Overall, 35 (28.5%) patients had experienced MG crisis and two died. More than half of the MG crisis episodes occurred beyond 2 years from clinical onset. Moderate-to-severe weakness at clinical onset (OR=5.79; 95% CI, 1.29-25.96, P=0.022) and presence of major co-morbid illness (OR=3.70; 95% CI, 1.29-10.65; P=0.015) were independent predictors for development of MG crisis. Serum/plasma levels of interleukin-17A and interferon-γ were higher in patients in MG exacerbation or crisis.
Conclusions: Long-term outcome of gMG among Hong Kong Chinese is satisfactory and use of immunosuppressive therapies especially azathioprine is crucial. MG crisis remains an important potentially fatal complication and is unexpectedly common even in the later course of disease.

Factors Affecting Motor Deterioration in Acute Deep White Matter Infarction

DH 7

Moamina Ismail
Division of Neurology, Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR

Background: A substantial number of patients with acute deep white matter infarction suffered from progressive motor deficits. This study aimed to determine its predictors, so as to generate hypothesis of the underlying pathogenesis and potential preventive or therapeutic strategies.
Methods: A total of 54 patients with acute deep white matter infarction were prospectively evaluated by daily National Institutes of Health Stroke Scale (NIHSS) motor score. Motor deterioration was defined as a drop in NIHSS motor score of ≥1 point during the first 7 days. Patients with and without motor deterioration were compared of their clinical and radiological parameters.
Results: Of the patients, 11 (20.4%) had motor deterioration. They had higher mean diastolic blood pressure in the first 24 hours (88.1 ± 17.2 mm Hg vs 79.0 ± 10.9 mm Hg; P=0.033), elevated haemoglobin level (14.6 ± 1.2 g/dL vs 13.2 ± 1.6 g/dL; P=0.007), elevated haematocrit level (0.433 ± 0.035 vs 0.392 ± 0.043; P=0.005), elevated white cell count (7.1 [6.0-7.9] x 10^9 /L vs 8.5 [7.3-9.2] x 10^9 /L; P=0.025), elevated total protein (73 [70-75] g/L vs 76 [73-81] g/L; P=0.03), elevated total cholesterol level (5.5 ± 1.5 mmol/L vs 4.6 ± 1.0 mmol/L; P=0.01), elevated low-density lipoprotein (LDL) cholesterol level (3.6 ± 1.3 mmol/L vs 2.7 ± 0.8 mmol/L; P=0.005), and elevated urine albumin-to-creatinine ratio (5.1 [2.0-8.4] mg/mmol vs 1.45 [0.7-2.6] mg/mmol; P=0.019). After logistic regression analysis, LDL cholesterol higher than 3.2 mmol/L (relative risk=11.85; 95% confidence interval [CI], 1.95-72.09; P=0.007) and urine albumin-to-creatinine ratio higher than 3.5 (relative risk=8.02; 95% CI, 1.32-48.8; P=0.024) were independent predictive factors for progressive motor deterioration.
Conclusion: Progressive motor deterioration in acute deep white matter infarction was independently associated with elevated LDL cholesterol and urine albumin-to-creatinine ratio, supporting the role of endothelial dysfunction as the underlying mechanism of such deterioration.

Therapy for Multiple Sclerosis: the Evidence, the News and the Future

S 1

Andrew Chan
Ruhr-University Bochum, Germany

During the past 20 years the therapeutic armamentarium in relapsing multiple sclerosis (MS) has considerably increased. Whereas newly introduced oral first-line treatment options offer more convenient application, injectable medications have the advantage of proven long-term efficacy and safety. This is particularly well demonstrated in vulnerable patient groups, eg children with MS or in females that may become pregnant under treatment. Therefore, more recent advancements of injectable treatment options, eg with minimisation of the burden of injections, are prudent. In theory, combination of agents with different modes of action should offer superior efficacy; however, in large this expectation was not met in clinical studies which highlight pleiotropic mechanisms of action. This is also reflected in the safety profile of therapeutic monoclonal antibodies: initially coined as "magic bullets" with highly specific drug targets, the occurrence of previously not anticipated adverse drug reactions illustrate our incomplete understanding of immune networks. Still, taking advantage of the variety of treatment options available in clinical practice, the scientific concept of "disease activity free status" appears to be attainable at least for a proportion of patients. Nevertheless, treatment algorithms are becoming more complex since aspects such as sequence of treatment, biological half-life or wash out between different agents have also to be taken into account. Despite developments in the treatment of relapsing MS forms over the past decades, treatment options for chronic disease are still rather limited, and neuroprotective approaches in the experimental phase. Thus, in addition to development of new therapeutic approaches, new study outcome parameters especially for chronic disease phases as well as valid biomarkers for assessment of individual risk-benefit profiles are urgently needed. Studies addressing these aspects are in their validation phase, and despite setbacks may lead to more individualised treatment approaches based on immunopathology, disease stage, and individual risk profile.

Brain Volume Loss in Multiple Sclerosis: Implications on Clinical Outcomes

S 2

Sven Schippling
Neuroimmunology and Multiple Sclerosis Research Section (NIMS), Department of Neurology, University Medical Center Zurich, Switzerland

Multiple sclerosis (MS) is a heterogeneous disease in which several environmental factors act on the basis of a complex genetic trait. Next to inflammation, driven by autoreactive, myelin-directed T-cells, tissue degeneration appears to be the second main driver of MS pathology. Furthermore, the loss in axonal density as well as neuronal degeneration have been identified as the structural homologue of functional deficits and sustained disability progression in MS.

The most appropriate way of quantifying the amount of structural damage in MS patients in vivo is magnetic resonance imaging (MRI). Global and focal measures of brain volume loss can be derived from high-resolution T1-weighted images that have become part of routine imaging protocols in MS over recent years. Methodological limitations have long been limiting the value of MRI atrophy assessment in MS. However, with the availability of recent MRI technology, including higher field strengths and improved post processing tools, atrophy can now be assessed reliably, provided that patients are scanned with systematic protocols on the same platform in exact repositioning. Still, the cellular or molecular basis of brain atrophy in MS is poorly understood.

Methodological limitations of MRI brain atrophy measures and how to overcome these will be critically reviewed in this presentation. Evidence for the clinical relevance of focal and global brain volume loss will be presented as well as data from recent clinical trials on treatment effects of Fingolimod and other therapies on brain atrophy outcomes.

Serial Electrophysiological Study of Guillain-Barré Syndrome

S 3

Liying Cui
Department Neurology, Peking Union Medical College Hospital, Neuroscience Center, Chinese Academy of Medical Sciences, Beijing 100730, China

Objective: To investigate the serial electrophysiological changes of acute inflammatory demyelinating polyneuropathies (AIDP) and acute motor axonal neuropathy (AMAN) through serial electrophysiological study of Guillain-Barré syndrome (GBS).

Methods: Prospectively, 21 GBS patients were recruited in Peking Union Medical College Hospital, and performed at least two serial electrophysiological tests around the second and fourth week after disease onset. Retrospectively, 21 GBS patients' records between 1997 and 2010 were collected; these patients had at least two serial electrophysiological recordings. The electrophysiological parameters included motor sensory nerve conduction, F waves, and electromyography. Serial electrophysiological changes of conduction block were analysed.

Results: In the first test, 26 (62%) of 42 patients fulfilled Hadden's criteria for AIDP, 10 (24%) patients for AMAN, and 6 (14%) patients were classified as equivocal. After follow-up, 17 (40%) patients were classified as AIDP, 16 (38%) patients as AMAN, 3 (7%) patients equivocal, and 6 patients with rapid electrophysiological recovery (classification unclear). In AIDP group, distal motor latency (DML) prolongation appeared at week 1 to 2, and became prominent at week 3 to 5; the nadir of distal compound muscle action potential (dCMAP) amplitude decrease occurred at week 1 to 2. In AIDP group, the early electrophysiological changes of F waves were decreased frequency with normal F wave latency, and F wave latency prolongation showed up later with nadir abnormality occurring at week 4. There were two patterns of CMAP amplitude recovery in AMAN group: rapid increase and persistent at low level, and the two different recovery patterns were found in different nerves of the same patient. The majority of classification changes were from AIDP and equivocal groups by initial electrophysiological tests. The main reason was the recognition by serial recordings of reversible conduction failure (5 patients), axonal degeneration (4 patients), and transient prolongation of DML (2 patients).

Conclusion: The clinical severity and prognosis of the AIDP and AMAN groups are similar. In some AMAN patients, the CMAP amplitude can rapidly increase, which could not be explained by axonal degeneration. Besides axonal degeneration, reversible conduction failure might be other underlying mechanisms of AMAN. The causes of classification changes after serial electrophysiological study include the length-dependent CMAP amplitude reduction, rapid resolve of conduction block, and transient prolongation of DML.

S 4

Physiology and Clinical Diagnosis of Amyotrophic Lateral Sclerosis and Related Diseases

Ryuji Kaji
Department of Neurology, University of Tokushima Graduate School of Medicine, Japan

Diagnosis of amyotrophic lateral sclerosis (ALS) is usually made on the basis of Airlie House revision of El Escorial criteria, which is often too late to initiate any putative therapies. We have proposed Awaji criteria for the earlier diagnosis of ALS, which put emphasis on the electrophysiological demonstration of fasciculations. The genesis of fasciculations is also investigated using various electrophysiological techniques, and are found significantly different between ALS and multifocal motor neuropathy mimicking ALS. In this talk, I will summarise the recent electrophysiological finding in ALS and related diseases.

Electroencephalography in Hong Kong: Teaching, Service, and Research

Howan Leung
Division of Neurology, Department of Medicine and Therapeutics, Prince of Wales Hospital, Hong Kong SAR

Electroencephalography (EEG) has been in use in Hong Kong since 1970s and there were many generations of development from electrodes wrapped in cloth and saline through to meshed hats using gel application. The electronic device has evolved from analogue to digital and from paper output to computer records. Over the years, local institutions, hospitals and professional societies have shouldered the clinical responsibility for EEG teaching and technician training. Certification and formalised training are anticipated in the near future for quality assurance and standard setting. Many aspects of EEG classification were undergoing revision. For example, the criteria for non-convulsive status epilepticus were updated according to the American Clinical Neurophysiology Society[1]: periodic discharges of >2.5 Hz or periodic discharges of ≤2.5 Hz or >0.5 Hz plus one of the following: EEG + clinical improvement with intravenous antiepileptic drugs, subtle ictal phenomenon or typical spatiotemporal evolution. The EEG as a clinical service is increasing in utility, although resource allocation may vary with regional difference. Early EEG in the first 48 hours after seizure may increase the diagnostic yield. Video EEG may help with the localisation and lateralisation of patients suffering from refractory partial-onset epilepsy using ictal and interictal information. In selected cases, where hypothesis-driven intracranial implantation is undertaken, the judicious use of intracranial EEG may help identify the seizure-onset zone and guide the necessary resection as part of epilepsy surgery. From a research point of view, high-frequency oscillations (HFOs), which have been identified and described in the literature during the interictal and ictal phases of patients with intracranial monitoring, may potentially point towards an epileptogenic zone. Studies have shown that the resection of HFO-generating cortices may lead to better surgical outcomes.[2-4] HFOs in the range of 80 to 250 Hz are known as ripples, whereas those in the range of 250 to 500 Hz are called fast-ripples. Studies on HFOs in the local population may help with future development of this modality of investigation.

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The Role of Immunology in Neuromuscular Junction Diseases

S 6

Angela Vincent
Nuffield Department of Clinical Neurosciences, University of Oxford, United Kingdom

In the 1970s, myasthenia gravis (MG) was shown to be caused by antibodies to acetylcholine receptors (AChRs). In 2001, antibodies to muscle-specific tyrosine kinase (MuSK) were found in some of the MG patients negative for AChR antibodies, and more recently antibodies to LRP4 in a small number. MuSK and LRP4 are postsynaptic membrane proteins that are responsible for the agrin-induced clustering of the AChRs at the neuromuscular junction. However, despite the importance of these findings and their clinical relevance, there are challenges in fully understanding the mechanisms of these diseases. In particular, the distribution and fluctuation of muscle weakness in AChR-MG, and the distribution and muscle atrophy in MuSK-MG require further investigation.

The main pathogenic hallmark of AChR-MG is loss of AChR numbers or function, with the resulting decrease in the endplate potentials. Some patients are negative for all known antibodies, but a proportion of these can be shown to have antibodies that only bind detectably to clustered AChRs, emphasising the importance of clustering of receptors for synaptic function in general. The mechanisms of AChR antibodies include divalent antibody-mediated internalisation of AChRs, complement-mediated lysis of the postsynaptic membrane, and varying extents of direct inhibition of AChR function. The weakness is caused by failure of the endplate potential to reach the critical threshold for activation of the compound muscle action potential.

MuSK antibodies are associated with a disease which is often predominantly ocular/bulbar and difficult to treat effectively. MuSK-MG is relatively rare in Northern Europe and Canada but appears to be present in up to 50% of patients without AChR antibodies in Southern Europe, and the equivalent US and Asian countries. MuSK antibodies have been shown to transfer disease to mice, but it is still not entirely clear how binding of MuSK antibodies to MuSK leads to neuromuscular transmission failure. MuSK antibodies can be shown to inhibit agrin-induced LRP4-MuSK interaction with downstream consequences for the stability of AChR clusters at the NMJ. However, the intracellular events that accompany these processes are not at all clear and require further work for a full understanding of the disease.

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Multiple Sclerosis Treatment Strategy for Long-term Clinical Outcome

S 7

Sven Schippling
Neuroimmunology and Multiple Sclerosis Research Section (NIMS), Department of Neurology, University Medical Center Zurich, Switzerland

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system. Whereas relapsing remitting phenotypes are characterised by inflammatory episodes that manifest as acute inflammatory lesions on brain or spinal cord magnetic resonance imaging (MRI) and, partly, as clinical relapses, progressive forms of the disease are commonly defined by slow but sustained disability progression. Inflammation in MS is driven by autoreactive, myelin-directed T-cells. The main driver of disability in patients with MS, however, is neuroaxonal degeneration appearing secondary to inflammation or even independent thereof.

Recent epidemiological as well as evidence from imaging studies suggests that tissue loss beyond the level related to physiological ageing does not exclusively characterise advanced disease stages, but can be detected as early as in cases with a first episode suggestive of MS, the so-called clinically isolated syndrome (CIS). Most, if not all, of the available treatments target the inflammatory component of the disease and treatment of progressive MS and the underlying tissue loss remains an unmet need in MS care. As a consequence, there is increasing consensus that treatment should be initiated early (eg in cases of CIS) and maintained throughout the relapsing phase of the disease.

MRI, as well as clinical markers, can assist in predicting disease evolution on a group level, they fail, however, in predicting individual patient outcomes. Also, biomarkers to assess or even predict treatment response on a single subject level do not exist. Treatment optimisation guidelines—becoming increasingly relevant in a rapidly evolving therapeutic MS landscape—should therefore consider available evidence of treatment non-response and be consented among MS experts in order to provide real-world evidence where data from controlled treatment optimisation trials are scarce.

Testing for Neutralising Antibodies to Interferon-beta in Patients with Multiple Sclerosis

S 8

WK Ip
Division of Clinical Immunology, Department of Pathology and Clinical Biochemistry, Queen Mary Hospital, Hong Kong SAR

Multiple sclerosis (MS) is the most common autoimmune inflammatory demyelinating disease affecting the central nervous system, leading to disability in young adults. Interferon-β (IFN-β) is the first-line treatment for relapsing-remitting MS. Unfortunately, development of neutralising antibodies (NABs) in these MS patients during treatment has been reported in recent years. These NABs will lower the biological activity of IFN-β and be associated with disease relapse and progression. Testing for these NABs has significant prognostic value on IFN-β therapeutic efficacy. However, there is no standardised assay for measuring NABs. Two NAB assays, the cytopathic effect assay (CPE) and the myxovirus resistance protein A (MxA) induction assay, are the most commonly used methods for the detection of NABs in clinical laboratories. Fewer studies have tried to evaluate an alternative method on detection of INF-β–induced *MxA* gene by real-time polymerase chain reaction quantification. In recent years, a cell-based luciferase reporter gene assay has also been developed and introduced for clinical studies. In this talk, the various bioassays for the detection of NABs against IFN-β will be described and discussed with some preliminary results from a local study.

Full Analyses of New Oral Anticoagulants in Atrial Fibrillation: Global Versus Asian

S 9

Chern-En Chiang
General Clinical Research Center, Division of Cardiology, Taipei Veterans General Hospital and National Yang-Ming University, Taipei, Taiwan

Atrial fibrillation (AF) is a major burden in Asia with a reported prevalence of 1%. By the year 2050, an estimated 49 million men and 23 million women in Asia will have AF. It is estimated that 2.9 million Asians will suffer from AF-associated stroke each year by 2050. With the projected increase in AF burden in Asia, stroke prevention in AF patients is highly important. While the CHADS2 score has been used to determine stroke risk and identify patients who need anticoagulation, the CHA2DS2-VASC (Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65-74 years, Sex category) score is potentially better in describing both patients who need and do not need anticoagulation treatment. With a similar CHADS2 score, Asians have a higher risk of stroke than non-Asians when receiving oral anticoagulants. Asians also have a higher risk of bleeding than non-Asians. Under warfarin treatment, all bleeding events—including gastrointestinal (GI) bleeding, intracranial haemorrhage (ICH) and haemorrhagic stroke—were higher among RE-LY Asian patients than non-Asians.

New oral anticoagulants (NOACs) are effective and safe alternatives to warfarin. In Asian RE-LY patients, dabigatran 150 mg twice a day showed superiority over warfarin in reducing rates of stroke and systemic embolism (1.39 vs 3.06% per year; hazard ratio [HR]=0.45). Dabigatran 110 mg twice a day also lowered the rate of stroke, but the difference between warfarin was not significant (HR=0.81). The benefits from NOACs, especially dabigatran, appear to be supported when the number needed to treat (NNT) to prevent a stroke or systemic embolism, and the number needed to harm (NNH) to produce an ICH, are calculated.

Full analyses of the Asian data in four randomised trials of NOACs (RE-LY, ROCKET AF, ARISTOTLE, and ENGAGE AF) will be presented in this talk.

Action-observation in Upper Limb Stroke Rehabilitation in Sub-acute Phase

S 10

Marco Franceschini
Neuro-Rehabilitation Department, IRCCS San Raffaele, Pisana – Rome, Italy

Background: The recovery of arm function in stroke patients presents limited results. Some studies demonstrated the presence in the human brain of a mirror neuron networks with the property to discharge during the observation of hand/arm functional actions (AO). In our two recent randomised controlled trials (RCTs), we showed the efficacy of AO in recovering dexterity and enhancing the beneficial effects of motor training in left hemiparetic patients in sub-acute stroke.

Methods: First RCT included 102 patients and second 67 divided in right (18 EG vs 19 CG) and left (15 EG vs 15 CG) brain lesion. All subjects were at the first acute stroke and the EG underwent vision of video sequences showing upper limb daily activities; CG watched a static image. Assessments were taken with: Fugl Meyer, Frenchay Arm Test, Box and Block (B&B), B. I. and FIM administered before (T0) and after the treatment (T1), and at follow-up (T2).

Results: In the first study, the analysis demonstrated a significant 'time for treatment' effect which was shown in the B&B test, favouring a higher impact of experimental treatment on upper limb recovery ($P<0.001$). In the second study the comparison of patients in all scales between EG and CG with left brain lesion did not present any significant difference. Differently the comparison between EG and CG with right brain lesion showed a significant improvement in EG for B&B (at T1 and T2) and for FIM Motor (at T1).

Conclusion: These studies confirm the efficacy of this new rehabilitation add-on approach regarding upper limb dexterity. A new aspect arising from this analysis would seem to be the importance of the role played by the left brain cortical area in plasticity reorganisation and upper limb recovery. Future RCT with neurophysiological assessment could be conducted in order to confirm this hypothesis.

S 11

Hybrid Assistive Neuromuscular Dynamic Stimulation (HANDS) Therapy: New Therapeutic Strategy for Hemiparetic Upper Extremity After Stroke

Toshiyuki Fujiwara
Department of Rehabilitation Medicine, Tokai University School of Medicine, Japan

We devised a therapeutic approach to facilitate the use of the paretic upper extremity (UE) in daily life by combining integrated volitional control electrical stimulation (IVES) with a wrist splint, the hybrid assistive neuromuscular dynamic stimulation (HANDS) therapy. IVES can change its stimulation intensity in direct proportion to the changes in voluntary generated EMG amplitude recorded with surface electrodes placed on the target muscle. The stimulation was applied to the paretic finger extensors. Using this assistive stimulation combined with a splint, patients with moderate-to-severe hemiparesis, who cannot extend their paretic fingers voluntarily, could extend their fingers at their will. Patients wore a wrist-hand splint and carried a portable IVES in an arm-holder for 8 hours during the daytime. The system was active for 8 hours, patients were instructed to use their paretic hand as much as possible. HANDS therapy was conducted for 3 weeks. The patients were also instructed to practise bi-manual activities in their daily lives. To examine the effects of the HANDS system, a randomised controlled trial was conducted with stroke patients. Furthermore, we studied changes in selected markers of brain and spinal plasticity induced by HANDS therapy. The paretic UE motor function improved after 3 weeks of HANDS therapy. Neurophysiologically, the intervention induced restoration of presynaptic and long loop inhibitory connections. Paired-pulse transcranial magnetic stimulation study indicated plastic change in the affected hemisphere. Functional improvement of UE motor function and spasticity induced with HANDS therapy are based on the disinhibition of affected hemisphere and modulation of reciprocal inhibition. The HANDS therapy may offer a promising option for the management of the paretic UE in patients with stroke.

S 12

Challenges and Opportunities in Drug Discovery for Neurodegenerative Diseases

Bai Lu
Tsinghua University Medical School, China

Despite huge progresses in neuroscience research, the number of approved drugs remains unchanged. Neurodegeneration (ND) is one of the most challenging areas in drug discovery. This is not only because brain is the most complex organ in the body, but also there is significant shortage of knowledge on disease biology. For example, the aetiology of Alzheimer's disease (AD) and Parkinson's disease (PD) is far from being understood. Central nervous system (CNS) drugs are known to have high attrition rate. Compared with other medicines, CNS drugs need to pass blood-brain barriers, a daunting task for drug development. Moreover, there is no good animal model that could be used to monitor disease progression or drug efficacy. In addition, lack of genuine biomarker and good clinical readout for AD or PD makes it extremely challenging for proof of concept studies in human.

To meet the challenges in ND drug discovery, many different approaches have been attempted in the academia and biopharmaceutical industry. Increasing evidence suggests that synapse and circuit dysfunctions underlying the pathophysiology of major brain illnesses. Studies of brain-derived neurotrophic factor (BDNF), the best known 'synaptogenic' molecule proven in human, may pave the way for a paradigm shift in treating psychiatric disorders. Emerging evidence on BDNF regulation of memory and emotion, the impact of BDNF genotype on psychiatric endophenotypes, and the progress in tools to measure synaptic dysfunction in humans all suggest that time is ripe to target synaptic repair by the BDNF pathway in the clinic. In this talk, I will highlight evidence for BDNF regulation of synaptic plasticity and synaptogenesis, and its role in cognitive functions such as memory and extinction. I will then discuss our recent work on translating BDNF biology into clinic. Specifically, I will talk about (1) efforts in developing measures of synaptic changes in human brain in vivo; and (2) possibilities in using BDNF val/met polymorphism for patient stratification in clinical trials. Through experimental medicine in humans, we hope that a paradigm-shifting 'synaptic repair' strategy will bring innovative medicines for the treatment of psychiatric diseases.

Advanced Magnetic Resonance Imaging Techniques in the Evaluation of Preclinical Alzheimer's Disease

S 13

Lin Shi
Division of Neurology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR

Preclinical Alzheimer's disease (AD) is a newly recognised stage of the disease, in which key biological changes begin years—or even decades—before symptoms, but not yet caused any noticeable 'clinical' symptoms. Searching for non-invasive imaging biomarkers to identify preclinical AD is under intense research worldwide. Due to the free radicals of ionising radiation and versatile imaging capability, advanced magnetic resonance (MR) imaging techniques in combination with objective quantification techniques have huge potential to derive differential biomarkers for preclinical AD diagnosis. In this talk, the speaker will introduce current state-of-the-art research work on this topic and present the latest research work conducted within their research team. Though further verification from longitudinal and large-cohort studies is still needed, these research efforts contribute to the computation and selection of MR biomarkers for preclinical AD.

Cerebrovascular Disease, Amyloid Plaques, and Cognitive Impairment

S 14

Vincent Mok
Division of Neurology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR

Although deposition of amyloid plaques is a key pathological hallmark of Alzheimer's disease, autopsy studies show that amyloid plaques are also frequently found in non-demented elderly subjects. Recent autopsy studies suggest that concurrent presence of infarct may significantly enhance the manifestation of dementia. However, given the retrospective nature of autopsy study, firm conclusion cannot be drawn.

We utilised in-vivo Pittsburgh compound B positron emission tomography to evaluate the interaction between various cerebrovascular diseases and subjects harbouring amyloid plaques. We found that even a mild cerebrovascular event (eg transient ischaemic attack) was able to induce rapid cognitive deterioration in subjects harbouring amyloid plaques. Our findings provide further evidence on the interaction between cerebrovascular disease and amyloid plaques in causing dementia.

Stroke Prevention in Asian Atrial Fibrillation Patients

S 15

Ping-Wing Ng
Division of Neurology, Department of Medicine and Geriatrics, United Christian Hospital, Hong Kong SAR

With the ageing population and the increasing prevalence of atrial fibrillation with age, the incidence of cardioembolic stroke due to atrial fibrillation is rising. Atrial fibrillation strokes are important since they are usually more severe and carry a higher mortality. While anticoagulation had shown to be effective in reducing the risk of stroke by two thirds, the underuse of anticoagulation is particularly significant among Asian countries. Many physicians are cautious about the risk of intracranial bleeding while patients are also not favouring the therapy because of the need for regular blood checking and the restriction on dietary elements. There was belief that Chinese had a lower risk of suffering from atrial fibrillation and that these patients were less common to have stroke. Recent data have proved these to be wrong. It is important to find some agents to fill up this treatment gap. The newer generation of anticoagulants have been shown to be at less as effective as warfarin and are associated with lower incidence of intracranial bleeding. Whether these agents can help to provide safe anticoagulation for atrial fibrillation patients to prevent ischaemic stroke among Chinese, some questions have to be answered before we can be certained.

Diagnosis and Management of Non-convulsive Status Epilepticus

S 16

Jason KY Fong
Past President, Hong Kong Epilepsy Society, Hong Kong SAR

Non-convulsive status epilepticus (NCSE) is defined as a state of ongoing seizures (or non-recovery between) without convulsions for more than 30 minutes. A combination of clinical features (often subtle, eg sudden alteration in mental state ranging from impaired concentration, confusion, stupor to coma, mutism, refusal to eat, mini-myoclonus, and nystagmus) and electroencephalography (EEG) data (continuous EEG monitoring often required) is essential in making the diagnosis. Proposed EEG criteria are directed mainly for adult-onset NCSE as the EEG picture in paediatric population is fundamentally distinct from adults comprising various forms of epileptic encephalopathies, eg Lennox-Gastaut syndrome, West syndrome.

In this presentation, an update on the current diagnosis and treatment of adult-onset NCSE will be presented. Standard treatment usually consists of intravenous (IV) administration of a benzodiazepine followed by IV phenytoin or valproate but randomised controlled data are lacking. Ongoing trials and evidence for the use of new antiepileptic drugs (eg levetiracetam, lacosamide) will be discussed.

NCSE is a heterogeneous condition which can be sub-classified into typical absence status epilepticus (SE), complex partial SE (limbic or non-limbic), simple partial SE (aura continua), all of which carry a favourable prognosis and outcome. In contrast, NCSE in the postictal phase of generalised convulsive SE or subtle SE bear much resemblance to convulsive SE in terms of aetiology, treatment, and outcome. In addition, NCSE may overlap with other encephalopathies known as 'boundary syndromes' (comprising coma with epileptiform EEG changes, epileptic behavioural disturbance, drug-induced or metabolic encephalopathies with epileptiform EEG changes) of which a different treatment approach is necessary.

A few cases will also be presented to highlight the diagnostic and treatment aspects of NCSE commonly seen in clinical scenarios.

Gene Therapy in the Treatment of Epilepsy

S 17

Matthew Walker
Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, UCL, London and National Hospital for Neurology and Neurosurgery, Queen Square, London, United Kingdom

Approximately 30% of people with epilepsy do not fully respond to our present drugs and fewer than 10% of these people are suitable for curative epilepsy surgery. Very often people are declined for resective surgery, because the epileptic focus is too widespread or overlaps with eloquent cortex.

An alternative approach to resective surgery is the use of gene therapy to reduce the excitability of excitatory neurons or to increase the excitability of inhibitory neurons in the focus. There have been considerable advances in the development of viral vectors that self-inactivate and are not immunogenic, providing safe and effective methods for gene therapy. We have successfully used a lentiviral vector to overexpress an endogenous gene that encodes the potassium channel Kv1.1 and so have cured epilepsy in a model of focal neocortical epilepsy.

A different approach is to express proteins that can be modulated on demand. We have used optogenetic (the expression of channels and ion pumps that are activated by coloured light) in order to increase or decrease neuronal excitability in specific classes of neurons. Using a system in which an implanted light is activated when a seizure is detected, it is possible through optogenetics to suppress seizure activity. Rather than using light-sensitive proteins, receptors have been developed that are activated by specific drugs—Designer Receptors Exclusively Activated by Designer Drugs (DREADDs). Using gene therapy to express in the focus a DREADD that is sensitive to an otherwise inert synthetic ligand, clozapine-N-oxide (CNO), we have been able to suppress seizure activity by the administration of CNO.

Although human trials are some way off, there is a clear route to translation and it is likely that trials of gene therapy in the treatment of epilepsy will occur within the next decade.

Channelopathy and Pharmacoresistance

S 18

Wei-ping Liao
Institute of Neuroscience and The Second Affiliated Hospital of Guangzhou Medical University; Key Laboratory of Neurogenetics and Channelopathies of Guangdong Province and the Ministry of Education of China, Guangzhou 510260, China

In the passed two decades, findings in epilepsy genetics have greatly advanced our knowledge of epilepsy and provide us insights into the molecular bases and underlying mechanisms of epilepsy. It is found that pure epilepsies are associated with abnormalities of channels or channel-regulatory genes mostly. They appear to be either generalised or partial epilepsies in the majority. There are overlaps of genetic abnormalities among generalised epilepsies featured by absence, generalised tonic-clonic, or myoclonic seizures, suggesting a potentially common underlying mechanism. In contrast, genetic partial epilepsies appear relatively specific both clinically and genetically. The localised gene expression can be one of the explanations for the pathogenesis of partial epilepsies. There are few channel genes that produce pure epilepsies with both generalised and partial features, which present a complicated situation with potentially distinct mechanism that depends on the system involved, the functional defects of the mutants, and the regional-, cellular-, and subcellular-specific gene expression pattern. Understanding the molecular bases and mechanisms of different epilepsies will help us in considering classification and terminology of epilepsy, and potentially further in the management of epilepsies in clinical practice, especially when it is considered that many channels are targets of antiepileptic drugs (AEDs). The mechanism of two phenomena of seizure aggravated by AEDs, ie absence aggravated by GABAnergic AEDs and partial epilepsy with febrile seizures plus aggravated by sodium-blocker AEDs, will be discussed.

The Basic Science Underlying Dopamine Dysregulation Syndrome and Impulse Control Disorders in Parkinson's Disease and the Implications of These Phenomena on the Treatment

Andrew Evans
Movement Disorder Service, Department of Neurology, The Royal Melbourne Hospital, Parkville Victoria 3050, Australia

Parkinson's disease (PD) is a chronic progressive neurodegenerative disorder, the core neuropathological hallmark of which is the loss of the dopamine nigrostriatal pathway associated with the formation of α-synuclein-positive Lewy bodies. Dopamine depletion in the dorsal striatum results in the core motor features of PD, including bradykinesia and rigidity, once the degree of the main denervation has reached approximately 60%. Attention on the nigrostriatal dopamine system in PD is justified by the success of the dopamine precursor levodopa and other dopamine agonists in alleviating motor symptoms. However, a broad range of non-motor symptoms also complicate PD and encompass neuropsychiatric, autonomic, sensory, and sleep disturbances. Many of the non-motor symptoms reflect the evolution of non-dopamine lesions.

Conversely, the dopamine treatments used to ameliorate motor disability in PD can trigger, worsen, or be the primary cause of symptoms. Some of these medication-induced symptoms appear to be idiosyncratic, many are toxic or dose-related, and others may arise only after long-term exposure to dopamine replacement drugs, thus reflecting drug-induced neuroplastic changes.

Motor-related complications of dopamine replacement treatments are the best understood medication-induced phenomena and include the progressive shortening of the duration of response to dopamine replacement drugs (ie the development of wearing-off phenomena) and the development of abnormal involuntary movements called dyskinesias. It has recently become apparent that medication-induced symptoms also include a set of impulsive and compulsive behavioural pathologies that are linked by their repetitive, reward or incentive-based natures. These disabling behaviours may evolve some time after the initiation of dopamine replacement therapies and encompass impulse control disorders, punding, and compulsive medication use.

The neurobiological and molecular mechanisms of brain dopamine systems and related circuitry that lead to altered patterns of synaptic plasticity, ultimately leading to neuroplastic changes, and altering motor and other psychological processes will be discussed.

Pharmacotherapeutic approaches to the management of these psychomotor disorders are limited but successful management should aim to address neuroadaptive processes beyond the dopamine system that underlie these drug-induced psychomotor phenomena.

The Use of Parkinson's KinetiGraph Technology on Parkinson's Disease's Treatment

S 20

Andrew Evans
Movement Disorder Service, Department of Neurology, The Royal Melbourne Hospital, Parkville Victoria 3050, Australia

Global Kinetics Corporation (GKC) along with the Florey Neuroscience Institute (Melbourne, Australia) has developed the Parkinson's KinetiGraph (PKG) for objective, ambulatory assessment of bradykinesia and dyskinesia in Parkinson's disease (PD).

The PKG records a patient's movement continuously via a watch-like data logger which is worn by the patient at home for 10 days. The data logger also provides PD medication reminders (as prescribed) during the recording time, the patient then acknowledges (on the data logger) once they have taken the medication.

The PKG report provides clinicians with an assessment of a patient's clinical state which is objective, includes scaled measures of bradykinesia and dyskinesia, links symptom fluctuations with the timing of medication, is comparable over time, and allows assessment of a patient's symptoms at home during the activities of daily living.

In addition to the motor symptoms of PD, the PKG also provides markers associated with day time somnolence, possibility for impulsive behaviours, and self-reported medication compliance.

The PKG is a clinical decision support tool helping clinicians to further enhance the management of PD.

Pharmacological Treatments of Parkinson's Disease: the Concept of Once-daily Dopamine Agonist Therapy

S 21

Nobutaka Hattori
Department of Neurology, Juntendo University, Japan

Parkinson's disease (PD) is the second most common neurodegenerative disease. Recently, this disease could be considered not only one of movement disorders but also one of neuropsychiatric disorders. Thus, this disease could be recognised as a complex disease. We cannot cure this disease. However, symptomatic therapies can improve patient's quality of life. Since induction of levodopa, the dramatic improvement of prognosis has been observed so far. However, other medications (monoamine oxidase type B inhibitors [MAOBIs] and dopamine agonists) had been developed to avoid levodopa-related motor complication such as motor fluctuation and dyskinesia induced by levodopa therapies. In addition to these, several non-dopaminergic treatments are now in clinical use to treat motor symptoms of PD, or are being evaluated as potential therapies. Indeed, adenosine A2A antagonists, istradefylline, and the antiepileptic agent zonisamide can extend the duration of action of levodopa. In contrast, there has been strong evidence that levodopa and dopamine agonists are effective at all stages of PD. Moreover, dopamine agonists and drugs that block dopamine metabolism are also effective for motor fluctuation. Adherence to treatment is of importance in clinical practice as it determines therapeutic responses and medical decisions. There is a suggestion that, in general, increased tablet load with multiple daily intakes is associated with poorer compliance in PD, which is consistent with observations in other medical conditions. Based on the concept of avoiding poorer compliance, long-acting form of pramipexole as once-a-day formulation could be better than conventional one. Furthermore, long-acting form has benefit to nocturnal symptoms. Finally, long-acting one may ameliorate not only motor symptoms but also non-motor symptoms especially impulse control disorders. In my presentation, I will review pharmacological treatments for PD including long-acting dopamine agonists as once-daily formulation.

Clinical Characteristics of Unruptured Aneurysms in Migraineurs in Korea

P 1

MJ Oh, M Kim
Department of Neurology, Seoul National University Hospital, Seoul, South Korea

Background: Incidental aneurysms are occasionally found in primary headache. However, their characteristics or prognosis are unknown. The aneurysms are screened by a magnetic resonance angiography (MRA) in migraineurs. The features comparing to the previous literature are described.
Methods: Consecutive 1773 patients were screened for aneurysm by MRA, and further evaluation with transfemoral cerebral angiography (TFCA), or three-dimensional computed tomography (CT) angiography were performed. For each aneurismal evaluation, size in mm, number (single or multiple), shape, and locations were recorded. All subjects were interviewed and completed a self-reported questionnaire which contained questions on the diversity of headache quality, severity, location, frequency, onset, duration, familial and environmental factors, associated symptoms, and headache-related disabilities. They were grouped into unruptured aneurysms and migraineurs without aneurysm, and comparison was made.
Results: Unruptured aneurysms were detected in 3.6% (63/1773) with a mean age of 56.0 years and higher proportion in woman (87.3%). The mean size of aneurysm was 3.5 mm and locations were internal carotid artery (48.7%), middle cerebral artery (19.7%), posterior communicating artery (11.8%), anterior communicating artery (11.8%), and basilar artery (3.9%) in order. The questionnaire showed difference in 'aggravation by hormone therapy' (P=0.039) and 'had a migraine in younger age' (P=0.021), 'pain location' (P=0.025), 'double vision' (P=0.026).
Conclusions: Unruptured aneurysm in migraineurs appeared to be found more in women with hormonal therapy, suggesting the development of aneurysm is gender-related pathophysiology. However, other clinical points with a predictive value to screen the incidental aneurysm in migraineurs warrant further study.

Case Report: A Young Man with Anti-voltage-gated Potassium Channel (Anti-VGKC) Antibody–related Encephalitis Treated with Consecutive Therapeutic Plasma Exchange

P 2

WK Choy, WH Cheng, R Li, SY Liu, CM Cheung, HY Cho, BY Lo
Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

In the past decade, autoimmune neurological diseases are getting increasingly recognised with the identification of many pathological antibodies. Anti-voltage-gated potassium channel antibodies (anti-VGKC-Ab) target cell surface antigens, and cause hyperexcitability of the peripheral nervous system (PNS) and central nervous systems (CNS). PNS hyperexcitability usually manifests as disorders like Isaacs syndrome or cramp-fasciculation syndrome, while CNS hyperexcitability presents as encephalitis. Anti-VGKC-Ab–related limbic encephalitis (LE) typically affects patients over 50 years of age, and has a female preponderance. Cases with the anti-leucine-rich-glioma-inactivated-1 (LGI1) subtype usually have no underlying tumours, while a small proportion of those with the anti-contactin-associated-protein-like-2 (CASPR2) subtype may be associated with malignancy.

We report on a 32-year-old man who enjoyed good past health, and was admitted to Pamela Youde Nethersole Eastern Hospital for amnesia. He had difficulty in retaining short-term memory, and had episodes of confusion. He gradually developed profound confusion, and also had an episode of generalised tonic-clonic seizure. Stereotyped limb movements were noted, and an element of faciobrachial dystonic seizure activity. He had no fever all along, and lumbar puncture has been performed to rule out CNS infection. Magnetic resonance imaging of the brain showed T2 FLAIR signals over bilateral medial temporal lobes, and serum testing subsequently came back to be positive for the anti-VGKC-Ab. He was treated with intravenous immunoglobulin followed by high-dose pulse steroid. However, response was poor and he was eventually referred to haematology team for a course of therapeutic plasma exchange (TPE), which was done by the Spectra Optia cell separator. The patient showed marked improvement in his sensorium, and became oriented with significant improvement in memory. There were no complications from TPE and he was discharged with maintenance oral steroid. Our case illustrates that TPE is an effective and safe treatment for anti-VGKC-Ab–related LE.

Orbital Apex Syndrome Secondary to Herpes Zoster Infection

P 3

Adrian TH Hui, Holly HY Lam, Raymond CK Chan
Department of Medicine, United Christian Hospital, Hong Kong SAR

Orbital apex syndrome is a rare but serious manifestation of herpes zoster ophthalmicus, resulting in total ophthalmicus and visual loss. We therefore present a case of herpes zoster infection causing orbital apex syndrome.

An 85-year-old man with well-controlled diabetes was initially admitted for right orbital pain and temporal headache. Examination revealed right eye swelling and reduced visual acuity, yet normal movement of extra-ocular muscles. Later the right eye was erythematous with injection, and vesicular rash was seen over right V1 dermatome. Oral acyclovir was initiated for herpes zoster along with pregabalin for control of herpetic neuralgia. Initial non-contrast computed tomography brain showed right preorbital soft tissue swelling only. Over the next 2 weeks, he developed right eye complete ptosis with right cranial nerve II/III/IV/VI palsy. Magnetic resonance imaging of the brain and orbit with contrast showed increased T2 signal with abnormal enhancement over right lateral periorbital region, right medial and lateral rectus muscles, right optic nerve sheath and around the right optic nerve at the orbital apex region. Lumbar puncture revealed no evidence of infection with normal protein level, and cerebrospinal fluid was negative for varicella zoster virus. Visual-evoked potential showed right optic neuropathy. Intravenous pulse steroid was given and then switched to tapering dose of oral prednisolone. His herpetic lesions were completely healed but there was still residual impairment in extra-ocular eye movement despite systemic steroid and oral acyclovir.

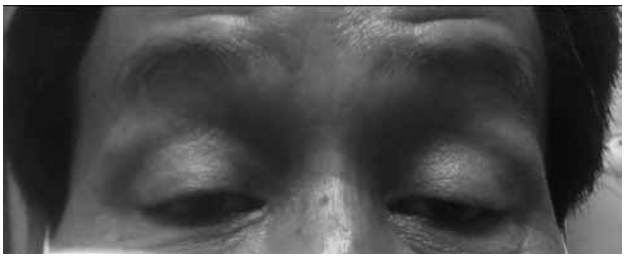
Total ophthalmoplegia can be due to compression of cranial nerves from periorbital oedema and direct viral spread. The use of systemic steroid helps improve the ophthalmoplegia but treatment course must be balanced with the response and patients' immunological state. Prognosis is variable, and the recovery is usually delayed.

P 4

Oculopharyngeal Muscular Dystrophy Masquerading as Chronic Progressive External Ophthalmoplegia

Siu-hung Li
Department of Medicine, North District Hospital, Hong Kong SAR

A 46-year-old man attended the neurology clinic at North District Hospital in 2001 because of bilateral droopy eyelids since the age of 44 years (fig). The degree of ptosis remained the same over years. He did not have any diplopia, limb weakness, speech, or swallowing difficulty. Examination revealed bilateral partial ptosis without fatigability. His pupils were normal and reactive to light. Extra-ocular eye movement was normal in all direction. His limb tone, power, reflex, coordination, and sensation remained normal. Mild degree of limitation in abduction and adduction of both eyes was noted in 2009. Investigations showed negative anti–acetylcholine receptor antibody, and normal renal and liver function test, muscle enzyme, thyroid function test, complete blood count, and fasting lactate level. Tensilon test and repetitive nerve stimulation were unremarkable. Muscle biopsy over right quadriceps was performed in 2001 showing normal findings on light microscopy. However, electron microscopic examination showed swollen mitochondria with hydropic matrix and loss of cristae. A few mitochondria exhibited paracrystalline inclusions which were present in the sarcoplasm outside and adjacent to the organelles. The pathological diagnosis was 'mitochondrial myopathy' and the clinical diagnosis of 'chronic progressive external ophthalmoplegia' (CPEO) was made. However, he has a family history of ptosis—both his mother and a younger sister have bilateral partial ptosis. An older brother and a younger sister are unremarkable. His daughters (aged 9 and 14 years) are also normal without ptosis. The features suggest autosomal dominant inheritance rather than maternal inheritance. He was referred for genetic testing. Oculopharyngeal muscular dystrophy (OPMD) is confirmed by genetic test because (PABPN1{NM_004643.3):c.[24_25ins(GCG)3GCA]+[=]; PABPN1{NP_004634.1}:p.[8_9ins4Ala]+[=] mutation is detected. This case illustrates that CPEO can mimic OPMD because of similar ocular abnormalities. Muscle biopsy in OPMD may show mitochrondrial abnormalities that may be mistaken as mitochondrial myopathy. In case of atypical pattern of inheritance, genetic test is helpful to differentiate between them.



Fig

Case Report: Acute Ophthalmoplegia Without Ataxia

P 5

SH Li, Sally MF Ip, Veronica TY Wai
Department of Medicine, North District Hospital, Hong Kong SAR

An 83-year-old woman with a history of post–radioactive I-131 (post-RAI) hypothyroidism was admitted to North District Hospital medical ward because of 1-day history of blurred vision and double vision. She did not have speech disturbance, limb weakness, or numbness. However, she had antecedent upper respiratory tract infection 1 week before onset. Examination revealed normal pupil size and response to light. Both eyes had limitation in abduction. Other cranial nerves were intact. Four limb tone, power, reflex, coordination, sensation, and gait were all unremarkable. However, she developed complete external ophthalmoplegia of both eyes few days after admission. Computed tomography (CT) brain on admission and CT brain and orbit with contrast and cerebral angiogram and venogram showed normal result. Blood tests for renal and liver function, complete blood count, thyroid function test, syphilis serology, immune markers (ENA, ANCA), and tumour markers (CEA, AFP) were all normal. Tensilon test and acetylcholine receptor antibody were negative. Cerebrospinal fluid (CSF) examination revealed mildly raised protein (0.77 g/dL) but other findings were normal. Acute ophthalmoplegia without ataxia (AOWA) was suspected based on the clinical findings and excluding alternative diagnoses. Intravenous immunoglobulin (IVIg) of 0.4 g/kg/day was given. Her ocular movement showed gradual improvement few days afterwards. Blood test for anti-GQ1b IgG was strongly positive and the diagnosis was confirmed. She had follow-up 5 weeks after onset and made complete recovery.

AOWA is rare and is one of the anti-GQ1b syndrome. This case fulfills the diagnostic criteria of AOWA.[1] Mandatory features include acute/subacute onset of external/internal ophthalmoplegia, absence of other neurological deficit such as ataxia or limb weakness, no other identifiable causes, and presence of anti-GQ1b IgG antibody. The supportive features are a history of infectious symptoms within 4 weeks before the onset of neurological symptoms, and CSF albuminocytological dissociation. Recognising this disorder allows early immunotherapy, eg IVIg treatment that may hasten recovery.

Reference

1. Lee SH, Lim GH, Kim JS, et al. Acute ophthalmoplegia (without ataxia) associated with anti-GQ1b antibody. Neurology 2008;71;426-9.

AUTHOR INDEX

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