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2nd Hong Kong Neurological Congress cum 24th Annual Scientific Meeting of The Hong Kong Neurological Society

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List of Speakers

Name	Affiliation
Prof Carl Bazil	College of Physicians and Surgeons at Columbia University, United States
Dr Carmen Kar-mun Chan	Hong Kong Eye Hospital, Hong Kong SAR
Dr Phoon-ping Chen	Alice Ho Miu Ling Nethersole Hospital / North District Hospital, Hong Kong SAR
Dr Andy Chi-on Cheng	Hong Kong Eye Hospital, Hong Kong SAR
Dr Alex Chi-ping Chow	Hong Kong Sanatorium & Hospital, Hong Kong SAR
Dr Kam-fuk Fok	Tuen Mun Hospital, Hong Kong SAR
Dr Ferdinand Hui	Cleveland Clinic Foundation, United States
Prof Jaseong Koo	Catholic University of Korea, Korea
Prof Eugene C Lai	The Methodist Neurological Institute, Houston, Texas, United States
Dr Joyce Lam	The Chinese University of Hong Kong, Hong Kong SAR
Dr Windsor Mak	Queen Mary Hospital, Hong Kong SAR
Dr Bik-ling Man	Tuen Mun Hospital, Hong Kong SAR
Dr Kin-ying Mok	UCL Institute of Neurology, United Kingdom
Prof Thomas Müller	St Joseph Hospital Berlin-Weissensee, Germany
Dr Kazunori Toyoda	National Cerebral and Cardiovascular Center, Osaka, Japan
Dr Tak-hong Tsoi	Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR
Prof David G Vossler	University of Washington, Seattle, United States
Prof Kyu-chang Wang	Seoul National University Hospital, Korea
Prof Shuu-jiun Wang	National Yang-Ming University School of Medicine, Taiwan
Prof Ruey-meei Robin Wu	National Taiwan University, Taiwan
Dr Liz Yuet-ping Yuen	The Chinese University of Hong Kong, Hong Kong SAR
Prof Nobuhiro Yuki	National University of Singapore, Singapore
Prof Ken KL Yung	Hong Kong Baptist University, Hong Kong SAR
Dr David S Zee	Johns Hopkins School of Medicine, United States

SCIENTIFIC PROGRAMME

Venue: Grand Ballroom, Level LL1, Kowloon Shangri-La Hotel

28 October 2011, Friday

		Function Room
09:00 – 09:30	Registration	
09:30 – 11:00	**FREE PAPER PRESENTATION** *Chairpersons: Thomas Leung, Winnie Wong*	**POSTER PRESENTATION**
11:00 – 11:20	Coffee Break	
11:20 – 12:30	**DISSERTATION HIGHLIGHTS** *Chairpersons: Thomas Leung, Winnie Wong*	
12:30 – 13:30	Lunch	
13:30 – 15:00	**SYMPOSIUM ON PERIPHERAL NEUROPATHY** *Chairpersons: Bun Sheng, Leonard Li*	
	Focal Neuropathies *Windsor Mak*	
	Guillain-Barré Syndrome: the Immunopathogenesis and Relationship between the Different Subtypes *Nobuhiro Yuki*	
	Common Pitfalls in the Electrodiagnosis of Entrapment Neuropathy *Alex CP Chow*	
15:00 – 15:20	Coffee Break	
15:20 – 16:45	**SYMPOSIUM ON NEURO-OPHTHALMOLOGY** *Chairpersons: SH Ng, Nelson YF Cheung*	
	Idiopathic Intracranial Hypertension *BL Man*	
	Atypical Optic Neuritis *Carmen KM Chan, Andy CO Cheng*	
	Using Eye Movements for Topological Diagnosis of Central Disorders *David S Zee*	

29 October 2011, Saturday

Function Room

POSTER PRESENTATION

09:00 – 09:30	Registration
09:30 – 09:40	**OPENING CEREMONY** Welcome Remarks: *Dr Leonard SW Li* President of the Hong Kong Neurological Society Guest of Honour: *Mr Richard MF Yuen, JP* Permanent Secretary for Food and Health (Health)
09:40 – 10:45	**NOVARTIS SYMPOSIUM ON MOVEMENT DISORDERS JOINT SYMPOSIUM WITH THE HONG KONG MOVEMENT DISORDER SOCIETY** *Chairpersons: Mandy Au Yeung, KL Tsang* **New Targets for Treatments of Parkinson's Disease** *Ken KL Yung* **Levodopa/carbidopa/entacapone as First-line Levodopa Formulation: Pharmacokinetic Considerations** *Thomas Müller*
10:45 – 11:00	Coffee Break
11:00 – 12:35	**NOVARTIS SYMPOSIUM ON MOVEMENT DISORDERS JOINT SYMPOSIUM WITH THE HONG KONG MOVEMENT DISORDER SOCIETY** *Chairpersons: Vincent Mok, XL Zhu* **Routine Genetic Screening for Young Onset / Familial Parkinson's Disease in Chinese—Are We Ready?** *Ruey-Meei Robin Wu* **Homocysteine and Entacapone Treatment** *Thomas Müller* **Deep Brain Stimulation for the Treatment of Parkinson's Disease** *Eugene C Lai*
12:35 – 13:30	Lunch
13:30 – 15:00	**ORIENT EUROPHARMA SYMPOSIUM ON EPILEPSY JOINT SYMPOSIUM WITH HONG KONG EPILEPSY SOCIETY** *Chairpersons: Colin Lui, Ada Yung* **Psychogenic Non-epileptic Seizures** *David G Vossler* **Upcoming Antiepileptic Drugs: the United States Experience** *David G Vossler*
15:00 – 15:20	Coffee Break
15:20 – 17:00	**GLAXOSMITHKLINE SYMPOSIUM ON EPILEPSY JOINT SYMPOSIUM WITH HONG KONG EPILEPSY SOCIETY** *Chairpersons: Eric Chan, Howan Leung* **Sleep and Epilepsy** *Carl Bazil* **Psychiatric Issues in Epileptic Disorders** *Joyce Lam*

30 October 2011, Sunday

		Function Room
09:00 – 09:30	Registration	
09:30 – 11:05	**SYMPOSIUM ON NEUROGENETICS** *Chairpersons: Jonas Yeung, YL Yu*	**POSTER PRESENTATION**
	Basic Neurogenetics: What Clinical Neurologists Need to Know *KY Mok*	
	Molecular Neurogenetics: Tools and Methods *Liz YP Yuen*	
	Advanced Neurogenetics: Frontiers in Research *KY Mok*	
11:05 – 11:20	Coffee Break	
11:20 – 12:35	**ALLERGAN SYMPOSIUM ON HEADACHE & PAIN** *Chairpersons: YW Chan, Edmund Woo*	
	Current Approach for Chronic Migraine Management *SJ Wang*	
	Updated Guidelines for Treatment of Neuropathic Pain *PP Chen*	
	Trigeminal Autonomic Cephalalgias *TH Tsoi*	
12:35 – 14:00	**BAYER LUNCH SYMPOSIUM** *Chairpersons: Patrick Li, PW Ng*	
	Anticoagulation for Prevention of Stroke in Patients with Atrial Fibrillation *Jaseong Koo*	
14:00 – 15:05	**SYMPOSIUM ON MOYAMOYA DISEASE JOINT SYMPOSIUM WITH THE HONG KONG STROKE SOCIETY** *Chairpersons: Dawson Fong, WC Fong*	
	Surgical Outcomes from Revascularisation Surgery for Moyamoya Disease: Experience in Tuen Mun Hospital, Hong Kong *KF Fok*	
	Surgical Management of Moyamoya Diseases *KC Wang*	
15:05 – 15:20	Coffee Break	
15:20 – 17:00	**SYMPOSIUM ON ISCHAEMIC STROKE JOINT SYMPOSIUM WITH THE HONG KONG STROKE SOCIETY** *Chairpersons: Raymand Lee, Sonny Hon*	
	Mechanical Thrombectomy in Ischemic Stroke: a Look at the Toolbox *Ferdinand Hui*	
	Medical Management of Intracranial Stenosis *Kazunori Toyoda*	
17:00	Closing Remarks and Presentation of Awards to Best Free Paper, Best Poster and Best Dissertation Presentations	

FP 1

3D Rotational Angiography as a Screening Imaging Test for Intracranial Stenting

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

Background: 3D rotational angiography (3DRA) is a new technique in delineating fine details of intracranial vasculature. We investigated the role of 3DRA in selecting patients for intracranial self-expandable stenting.
Methods: Patients who had strokes referrable to a high-grade symptomatic stenosis were recruited and underwent screening for intracranial stenting by a conventional digital subtraction angiography (DSA) and a 3DRA. Both imaging tests were performed by a biplane angiographic equipment (Allura Xper FD 20/20, Philips Medical Systems, Netherland). DSA consisted of anteroposterior, lateral and bilateral oblique views of the target artery with 10 mL of iopamiro 300 in each injection from a 4F H1 catheter positioned at internal carotid artery or vertebral artery ostium. By the same catheter and contrast, 3DRA was obtained by a rotating arm centred at the target lesion, comprising 120 images gathered over a scan time of 4 seconds. A radiologist blind to the patient's clinical information compared the anatomy of the lesion and its immediate vicinity as revealed by the two imaging methods. The degree of stenosis was measured by WASID technique. Lesion characteristics which might alter the decision of endovascular treatment were recorded.
Results: Paired DSA and 3DRA were obtained in 169 patients. The two methods were comparable in the measurement of the stenosis severity. However, among the four patients who had fenestrations mimicking or adjacent to the stenosis (middle cerebral artery=3; basilar arterty=1), three were only evident in 3DRA but not in convention DSA. In another three patients, angioplasty/stenting was precluded based on 3DRA which showed an adjacent perforator or branch with a highly stenosed ostium.
Conclusions: 3DRA may compare favourably with conventional DSA in depicting minute details of intracranial vascular anatomy, and is potentially useful in preoperative evaluation of intracranial angioplasty.

FP 2

Intravenous Alteplase for Ischaemic Stroke Patients with Borderline Eligibility in Hong Kong—How Selective Should We Be?

Alexander Lau[1], Edward Wong[1], Yannie Soo[1], Deyond Siu[2], Venus Hui[1], Edward Shum[1], Cecilia Leung[1], Colin Graham[3], Thomas Leung[1], Lawrence Wong[1]
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Background: Variance exists in selecting patients for stroke thrombolysis. Unlike US labelling, intravenous alteplase (IVTPA) is not recommended for age >80 years and NIHSS >25 by European guideline. Besides, both exclude patients >80 years or with a history of diabetes and stroke for the 3-4.5 hours window. We compared the outcomes of patients who received IVTPA outside these guidelines to those who complied, and to a control group.
Methods: Consecutive patients received IVTPA <4.5 hours between January 2007 and June 2011 at our centre were reviewed. Patients compliant to both guidelines were compared to those who did not. They were further compared to a control group with the same borderline eligibility but were not given IVTPA due to non-office hours admission between October 2008 and May 2011. Outcome measures were 3-month modified Rankin Scale (mRS) ≤2 and mortality, and symptomatic intracranial haemorrhage (SICH) according to ECASS (European Cooperative Acute Stroke Study).
Results: Fifty-four patients received IVTPA. Thirty-three were compliant to both guidelines and 21 were non-compliant. For non-compliant group (mean age 81.6±8.2, NIHSS 18.6±8.2), 16 were >80 years, 5 had NIHSS >25, and 2 thrombolysed between 3-4.5 hours had a history of both diabetes and stroke or >80 years. For comparison, 22 non-thrombolysed controls (mean age 77.0±10.9, NIHSS 19.1±10.1) were identified. Twenty (61%) of the compliant group versus 4 (19%) of the non-compliant and none of control groups attained 3-month mRS ≤2 (non-compliant vs control, P=0.05). Three-month mortality rates were 3%, 43% and 27% for compliant, non-compliant, and control groups respectively (non-compliant vs control, P=0.35). SICH occurred in one, two, and one patients of compliant, non-compliant and control groups, respectively.
Conclusions: The outcomes of patients given IVTPA outside both US and European guidelines had poorer outcomes compared to those who fulfilled. Still, those who were not given IVTPA fared even poorer. Further prospective randomised trials are needed to substantiate the use of IVTPA in borderline eligible patients.

FP 3

Subthalamic Deep Brain Stimulation for Advanced Parkinson's Disease: Efficacy and Complications

Movement Disorder Group, Prince of Wales Hospital, The Chinese University of Hong Kong; Anne Chan[1], Jonas HM Yeung[1], Danny TM Chan[2], XL Zhu[2], Edith Wong[2], KY Lau[2], Rosanna Wong[3], Christine Lau[1], Vincent CT Mok[1], Wayne WS Poon[2]
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Background: Deep brain stimulation (DBS) of subthalamic nucleus (STN) was first performed in Hong Kong since 1998 at our centre for patients with advanced Parkinson's disease (PD). We hereby report the efficacy and complications of STN DBS for advanced PD.
Methods: All PD patients who received STN DBS from September 1998 to January 2010 were included in the present analyses. We compared the Unified Parkinson's Disease Rating Scale (UPDRS) before and at least 2 months after the operation. Peri-operative complications were noted.
Results: A total of 41 PD patients (mean age, 54 years; 21 males) received bilateral STN DBS. The median follow-up duration was 12 months (range, 2-77 months). There was a significant overall improvement (31%; P<0.0001) in UPDRS in part III (motor performance) postoperatively at "on stimulation and off medication condition" compared with preoperatively at "off medication condition". There was also a significant improvement (32%, P<0.0001) in UPDRS part II (functional level) score. Peri-operative complications included lead fracture (n=1), and lead migration (n=1). There was no perioperative mortality.
Conclusions: Our efficacy and safety results were comparable to overseas centres. Overall, STN DBS is an effective and safe treatment for advanced PD.

FP 4

Guillain-Barré Syndrome: a Retrospective Study of Clinical Profiles and Outcomes in a Tertiary Centre

Anna HY Wong, YF Cheung, WC Fong, KW Fong, HF Chan, YW Ng, LT Chan, YC Chan, WT Lo, M Ismail, HM Chan, P Li
Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR

Background: Guillain-Barré Syndrome (GBS) is an acute peripheral neuropathy which is potentially fatal and debilitating. Effective treatment is available. Local data are scarce. In this study, we reviewed the clinical profiles and outcomes of GBS managed in a tertiary centre in Hong Kong.
Methods: A retrospective study was performed on GBS patients who met the Asbury and Cornblath (1990) diagnostic criteria and were admitted between July 2001 and December 2010 to the Department of Medicine, Queen Elizabeth Hospital. Data were analysed by PASW Statistics 18 software.
Results: We found 65 GBS patients within the study period; 44 (68%) were male. The mean age of onset was 61 (standard deviation, 15.7) years; 94% were Chinese. The number of patients diagnosed per year ranged from 3 to 13. Symptoms suggestive of antecedent upper respiratory tract infections (48%) and the gastrointestinal tract infections (11%) were recorded respectively. Twelve per cent of patients had a history of recent vaccination in the past 1 to 3 weeks. Presenting features included limb weakness (94%), facial weakness (10%), numbness (63%), visual symptoms (14%), bulbar symptoms (24%), hyporeflexia/areflexia (78%), ataxia (22%) and dysautonomia (27%). Similar to Caucasian series, acute inflammatory demyelinating polyradiculoneuropathy (AIDP) was the commonest subtype (57%), followed by axonal subtypes (AMAN or AMSAN, 21%), Fisher's syndrome (12%) and Bickerstaff brainstem encephalitis (2%). Around one-third received intensive care unit (ICU) care and one-fourth had respiratory failure requiring mechanical ventilation. Seventeen per cent of patients had temporary tracheostomy performed. For these selected populations, the mean length of ICU stay was 14 days (95% confidence interval [CI], 8.5-19.6) and the mean length of mechanical ventilation was 25.5 days (95% CI, 14.4-36.7). At 6 months, 84% of patients survived and 66% remained independent in activities of daily living (ADL), as measured by the Glasgow Outcome Scale. Using a multivariate logistic regression model with age, sex, antecedent infection/vaccination, bulbar presentation and disease subtype as covariates, age was the only prognostic factor that significantly determined the 6-month independency in ADL but not survival.
Conclusions: In our cohort, GBS carried significant morbidity and mortality. The only significant predictor was age in our model. Larger, multicentre studies are warranted for better delineation of clinical predictors of adverse outcomes.

FP 5

Stroke in Tuberculous Meningitis

YP Chu, MK Fong, B Sheng, YH Chan, WT Wong, KK Lau
Department of Medicine, Princess Margaret Hospital, Hong Kong SAR

Background: The objective of this study was to identify the predictors of stroke in patients with tuberculous meningitis (TBM) and their prognostic implications.
Methods: All patients with TBM in Princess Margaret Hospital from 2000 to 2010 were included in the study. Of the 34 patients with TBM, 16 patients developed stroke. Potential predictors of stroke including co-morbidities and biochemical findings were studied. Radiological examinations including computed tomography or magnetic resonance imaging brain were also studied. The neurological outcome measured was mortality rate and Modified Rankin Score at 6 months (0-3 vs 4-6).
Results: Patients with stroke were older (55.4 ± 15.2 vs 45.9 ± 16.6; P=0.09) and had lower cerebrospinal fluid (CSF)–to–serum glucose ratio (0.24 ± 0.14 vs 0.33 ± 0.14; P=0.09). There were less HIV patients in those with stroke (6.3% vs 22.2%; P=0.19). Most of the infarcts in TBM were multiple (87.5%), bilateral (62.5%), and located in basal ganglion (31.3%) and subcortical white matter (50%). Patients with stroke had a higher mortality rate (31.2% vs 11.15%; odds ratio [OR]=3.64; P=0.147) and more adverse neurological outcome at 6 months (56.2% vs 29.4%; OR=3.09; P=0.119). High CSF total protein (2.59 ± 1.3 vs 1.57 ± 0.53; P=0.0096) and older age (64 ± 13.2 vs 44.4 ± 14.5; P=0.014) were associated with adverse neurological outcome at 6 months in TBM patients with stroke.
Conclusion: Stroke is common in patients with TBM leading to a higher mortality and worse neurological outcome.

DH 1

Transient Axonal Glycoprotein-1 (TAG-1) Polymorphism and Its Correlation with Clinical Features and Prognosis in Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)

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

Background: Chronic inflammatory demyelinating polyradiculopathy (CIDP) is a heterogeneous group of acquired disorders characterised by peripheral nerve demyelination. Previous studies have shown a good response to immunotherapy but a significant proportion of patients continue to require maintenance therapy. A recent study identified a potential genetic marker for responsiveness to intravenous immunoglobulin (IVIG). In this study, CIDP patients were examined to look for association between clinical, electrophysiologic, genetic factors and treatment response as well as risk of treatment dependence.

Methods: Case records of 32 CIDP Chinese patients diagnosed between January 1995 and March 2010 at the three Neurology centres on Hong Kong Island (namely, Queen Mary Hospital, Pamela Youde Nethersole Eastern Hospital, and Ruttonjee Hospital) were reviewed to examine their clinical features, electrophysiologic parameters on presentation, disease course and outcome. Blood samples were available from 22 patients and 147 controls. DNA was extracted from peripheral leucocytes and the transient axonal glycoprotein 1 (TAG-1) genotype for the previously reported single nucleotide polymorphism (SNP) was determined using the Sequenom MassARRAY system.

Results: The overall response rate to immunotherapy with prednisolone, IVIG or plasma exchange (PE) was 80% with no difference detected among the three therapies. Clinical features such as age of onset, duration of symptoms, presence of diabetes mellitus (DM), presence of sensory symptoms and modified Rankin score (mRS) on presentation did not predict treatment responsiveness. Electrophysiologic parameters on the initial nerve conduction study were also not associated with treatment response. Fifty-eight percent of our patients were dependent on maintenance therapy after a mean follow-up period of 5.8 years. Clinical features such as age of onset, duration of symptoms and presence of DM were not predictive of treatment dependence. Patients with more prolonged distal motor latency (DML) in the upper limbs had a higher risk of treatment dependence (P=0.03, OR=1.03). Patients with a higher mean motor nerve conduction velocity (NCV) in the upper limbs showed a trend of lower risk of treatment dependence but this did not reach statistical significance. TAG-1 genotypes in 147 healthy controls and in 22 CIDP patients with regard to the SNP designated by rs2275697 were determined and no significant difference in allele frequency was detected. Furthermore, among CIDP patients, there was no association between TAG-1 genotype and age of onset, presence of DM, mode of onset and disease course. However, those who were homozygous for G had significantly more prolonged DML. Those with the G allele present (patients who were either homozygous for G or heterozygous with G/A) had significantly lower compound muscle action potential (CMAP) amplitude in the upper limbs and more prolonged DML in the lower limbs than those homozygous for A.

Conclusions: The overall treatment response rate in CIDP is high and even patients with advanced age, unfavourable electrophysiologic features and severe disability can improve with treatment. However, a significant proportion will require long-term maintenance therapy to prevent relapses. Patients whose initial nerve conduction study showed more prolonged DML in the upper limbs were at increased risk of being treatment dependent. The TAG-1 G allele was found to be associated with the severity of demyelination on the initial nerve conduction study in CIDP patients, which suggests a role of TAG-1 in the pathogenesis of demyelination.

DH 2

Usefulness of ABCD2 Score in Prediction of 90-day Risk of Stroke in Patients with Transient Ischaemic Attack in a Chinese, Non-tertiary Care Community Hospital

KK Wong
Department of Medicine and Geriatrics, Yan Chai Hospital, Hong Kong SAR

Background: Stroke was the second cause of mortality worldwide in 2004 and ranked the fourth cause of death in Hong Kong in 2008. It was frequently preceded by transient ischaemic attack (TIA). TIA is recognised to be a medical emergency because its risks of early stroke are high. Various clinical prediction tools are proposed to aid the risk stratification after TIA. The "ABCD2" scores are attempted to quantify this risk. Those with the highest scores have significantly increased risk of early stroke. These scores had been validated in several studies but were not universally successful in different populations.
Aim: The purpose of the study was to evaluate the ABCD2 score in patients with TIA and the risk of subsequent stroke in a local Chinese, non-tertiary community hospital.
Methods: From 1 January 2004 to 31 December 2009, all patients' records with principal diagnosis as 'transient ischaemic attack' (TIA) coded by ICD9 had been retrieved. Incidence of stroke among TIA patients had been identified at 90 days. All the baseline parameters were recorded. Incidence of stroke among TIA patients had been identified at 90 days. ABCD2 scores were calculated retrospectively. From the differential stroke incidence, the patients with TIA have been divided into two groups with different ABCD2 scores for further statistical computation. Primary outcome was stroke within 90 days after TIA. Secondary outcomes are cardiovascular diseases including recurrent TIA or acute stroke, cardiovascular disease and death.
Results: There were a total of 446 patients with diagnosis of TIA recruited. Of them, 23 (5.4%) had been rejected. The total 90-day incidence of stroke in recruited patients was 5.2% (22 patients). More than half of the stroke recurrence occurred within 7 days (4 patients, 18%) and 30 days (9 patients, 41%) whereas the remaining (9 patients, 41%) were at 90 days. Patients were categorised into two groups with ABCD2 score at 5. There was significant difference in 90-day stroke incidence between high (16 patients, 72.7%) and low (6 patients, 27.3%) ABCD2 score (P=0.047). Odds ratio was 2.817. The Kaplan-Meier survival curve for 90-day stroke of dichotomised ABCD2 score at 5 was plotted. P value of log-rank test was 0.0295.
Conclusion: Our study has confirmed the usefulness of ABCD2 score in predicting the 90-day stroke risk in patients with TIA in a Chinese, non-tertiary local community hospital. Those with high ABCD2 score would be associated with higher 90-day stroke incidence. More resources should be allocated to those with higher ABCD2 score in TIA patients.

Clinical Profile and Prognosis of Patients with Myasthenia Gravis in Hong Kong

DH 3

Eric SW Yeung
Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

Background: Myasthenia gravis (MG) is the commonest neuromuscular junction disorder. Previous local studies reported an annual incidence of 4 per million, while latest western figures are much higher. With advances in treatment, the prognosis of MG patients has much improved in western countries over the past decades. However there is a scarcity of local data.

Objectives: Our study has four objectives: (1) to study demographics and clinical characteristics in patients with MG; (2) to examine the utilisation of various diagnostic modalities for MG; (3) to review our experience in management of the disease; and (4) to determine the clinical outcomes and prognosis of MG in Chinese patients.

Method: This is a retrospective review of patients with MG attending our Neurology unit of Pamela Youde Nethersole Eastern Hospital between 1 October 1993 and 31 December 2010. Patients were identified by the clinical data system (CDARS) with the diagnosis of MG, and divided into three groups (ocular, generalised, ocular to generalised) for comparison. Demographics, clinical profile, history of hospitalisation and intensive care unit care, myasthenic/cholinergic crisis, investigation results, treatment modalities, outcome at the time of analysis including functional status and mortality were retrieved from the clinical management system (CMS) and hospital charts for review and analysis. Factors associated with mortality, generalisation in ocular onset patients were studied.

Results: A total of 152 patients were identified. Two patients were lost to follow-up and excluded. The mean age at diagnosis was 51.18 (range, 13-91) years. A female predominance was noted in all age-groups. The annual incidence was 13.3 per million (range, 8.3-23.3). Ocular MG comprised the majority (59.3%). Fifteen patients had ocular onset and delayed generalisation of symptoms, all occurring within 30 (range, 1-30) months. Significant associated factors with generalisation included positive anti-acetylcholine receptor (anti-AChR) antibody, positive repetitive stimulation test (RST), and presence of pathologically confirmed thymoma. The anti-AChR antibody was the commonest test performed (92.7%) while Tensilon test had the highest positive rate (75%). 25.5% of patients had thymoma on computed tomography (CT) scan of thorax. 91.3% of patients were on mestinon. 40.7% were on steroids. 39 patients required in-patient management of their MG exacerbation, leading to a mean hospital stay of 7.95 (range, 2-125 days). 22 patients had myasthenic crises, all occurring before treatment with standard immunotherapy. Thymectomy was done in 23 patients, with 19 pathologically confirmed thymomas. Four patients died of MG-related complications: three from respiratory failure and pneumonia, one from severe sepsis while on corticosteroid. The disease-related mortality was 2.7% over a mean disease duration of 9.65 (range, 1-51 years). No risk factor association with mortality was identified. All surviving patients achieved clinical remission, with modified Rankin Scale of 0 or 1.

Conclusion: MG was common in our locality, with an annual incidence comparable to western studies. None of the investigation modalities was satisfactory to serve as the "golden standard" for diagnosis. Utilisation of current pharmacological options was adequate, but thymectomy was less considered. Prognosis is good in our group, comparable to western countries and previous local experience.

DH 4

Factors Associated with the Risk of Thymoma at the Presentation of Myasthenia Gravis

KY Cheung
Department of Medicine, Tuen Mun Hospital, Hong Kong SAR

Background: Thymoma is found in 10 to 15% of patients with myasthenia gravis (MG). Thymoma-associated MG is considered to be a more severe disease and all thymoma patients are indicated for thymectomy. It is unclear whether certain clinical or serological findings of MG patients at the time or early after the diagnosis can predict the presence of thymoma.
Objective: To determine the demographic, clinical as well as autoimmune antibody characteristics that may differentiate between thymoma-associated MG and non-thymoma–associated MG in the early course of the disease. Comparison for the clinical courses during the whole follow-up period of MG patients with or without thymoma was also made.
Methods: We retrospectively evaluated MG patients followed up at Tuen Mun Hospital in Hong Kong from year 2000 to 2010. MG was diagnosed by the typical history and signs of fluctuating and fatigable muscle weakness with its associations with the following variables: the titre of anti-acetylcholine receptor antibody, an unequivocal clinical improvement in response to anticholinesterase inhibitors, and a decremental pattern on repetitive nerve stimulation test and the status of thymoma on imaging study. The baseline characteristics, clinical presentation, courses of disease during the early and the whole follow-up periods, treatments offered, anti-acetylcholine autoantibody titers as well as the other associated autoimmune diseases were recorded and compared between the groups with or without thymoma.
Results: A total of 184 MG patients who fulfilled the criteria were identified and followed up. Thymoma was diagnosed in 19.6% of them. The mean age of patients with thymoma was older (55.08 vs 44.56; P=0.042); female sex was more prevalent (female vs male ratio of 1.4 vs 1) but the sex ratio was similar when compared with those without thymoma. Although the presenting symptoms and baseline MGFA scores were similar, thymoma-associated patients had a significantly more rapid deterioration of MG and more severe disease with higher mean of maximum MGFA score (2.81 vs 1.26; P<0.001) within the first 6 months of follow-up, and were also more likely to develop generalised MG eventually (83.3% vs 38.5%; P<0.001) when compared with non-thymoma group. All thymoma patients had positive anti-acetylcholine receptor antibody and a higher titre was recorded. Their long-term outcome was comparable to non-thymoma–associated MG patients with similar MGFA score on last follow-up. Autoimmune disease was present in 37% of patients overall with thyroid disease being the commonest association. Using multivariate logistic regression model, a high MGFA score at 6 months (MGFA 3-5) and a very high anti-AChR titre (>19 nmol/L) were predictive of thymoma.
Conclusion: MG patients at risk of thymoma could be identified during the early course of the disease. A high MGFA score at 6 months and a very high anti-AChR titre predicted the occurrence of thymoma.

DH 5

Predictors of Early Neurological Deterioration During Acute Phase of Ischaemic Stroke: Experience in Acute Stroke Unit at a Regional Hospital in Hong Kong

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Background: Patients suffering from acute ischaemic stroke are at risk of neurological deterioration within the first few days after stroke onset. The frequency, clinical characteristics and contributing factors of early neurological deterioration during the acute phase of ischaemic stroke in a local hospital in Hong Kong were investigated.
Methods: Consecutive acute ischaemic stroke patients admitted to the Acute Stroke Unit at Tuen Mun Hospital, a major regional hospital located in the New Territories West, Hong Kong were studied prospectively. Demographical characteristics, clinical parameters, computed tomographic (CT) brain findings and laboratory results were evaluated. The National Institute of Health Stroke Scale (NIHSS) was used to assess stroke severity and neurological deficits. Assessments using NIHSS were performed at baseline and after admission. Early neurological deterioration was defined as an increase in NIHSS score by 4 or more points from baseline within 7 days from stroke onset.
Results: A total of 110 acute ischaemic stroke patients were recruited, of whom 27 (24.5%) suffered from early neurological deterioration. The predictive factors of early neurological deterioration included a high baseline NIHSS score (P<0.001), low Glasgow Coma Scale score on admission (P<0.001), and baseline CT brain findings of infarcts on corona radiata (P=0.024), territorial infarcts (P<0.001), cerebral oedema or pressure effects (P<0.001), hyperdense middle cerebral artery sign (P<0.001) and haemorrhagic infarcts (P=0.002). Cerebral small vessel disease (P<0.001) and lacunar infarcts on CT brain (P=0.001) were protective factors. Those who had early neurological deterioration were more likely to have died at 30 days (33.3% vs 1.2%; P<0.001) and had a longer length of hospital stay (24.3 days vs 13.8 days; P=0.025).
Conclusion: Early neurological deterioration in acute ischaemic stroke is common. It is associated with higher risk of early death and longer length of hospital stay. These patients may be identified early at their presentations. A great sense of awareness and prompt investigation and management are in need to prevent its occurrence.

S 1

Focal Neuropathies

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Focal neuropathy is a problem frequently encountered in clinical practice. Different patient groups tend to have different underlying aetiologies. Patients with diabetes mellitus can have acute mononeuropathy affecting the cranial as well as peripheral nerves. Besides, they are more prone to chronic entrapment neuropathies. Diabetic amyotrophy is also a focal problem but patients can present heterogeneously. Vasculitic mononeuropathy and mononeuropathy multiplex can be seen in some connective tissue diseases. This condition may also occur in isolation in the absence of extra-neural involvement. The electro- and histological diagnosis of vasculitic mononeuropathy multiplex will be discussed. Apart from diabetic patients, entrapment neuropathy at multiple sites can occur in hereditary neuropathy with liability to pressure palsies and at the early stage of Guillain-Barré syndrome. These models are illustrations of the double-crush phenomenon. Focal involvement can also be seen in motor neuropathy with multifocal motor conduction block and the CANOMAD syndrome, which are rare variants of chronic inflammatory demyelinating polyneuropathy.

S 2

Guillain-Barré Syndrome: the Immunopathogenesis and Relationship between the Different Subtypes

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The recent advances in Guillain-Barré syndrome research have improved our understanding of the relationship between the different subtypes. The three major subtypes are acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN) and Fisher syndrome, variations in the clinical presentations are likely to represent different ends of a continuous disease spectrum. AIDP, which frequently presents facial palsies and distal paresthesia, is associated with cytomegalovirus and Epstein-Barr virus infections. 'Facial diplegia and paresthesia' shows subclinical motor nerve demyelination in limbs and is associated with both infections, supporting that this is a regional form of AIDP. AMAN and Fisher syndrome are associated with *Campylobacter jejuni* enteritis. *C jejuni* sialyltransferase gene polymorphism determines the ganglioside-like lipo-oligosaccharide structure. GM1- or GD1a-like lipo-oligosaccharide induces anti-GM1 or -GD1a autoantibodies, causing AMAN; whereas, GQ1b-like lipo-oligosaccharides triggers anti-GQ1b antibodies causing Fisher syndrome. This suggests that AMAN and Fisher syndrome are part of the same disease spectrum along with the presence of overlapping cases of AMAN and Fisher syndrome. Depending on the severity of nerve insult in AMAN, this autoimmune attack causes the less extensive 'acute motor conduction block neuropathy' or more extensive 'acute motor-sensory axonal neuropathy' subtypes. Although typically associated with Fisher syndrome, anti-GQ1b autoantibodies are also associated with acute ophthalmoplegia without ataxia, isolated internal ophthalmoplegia, acute oropharyngeal palsy, ataxic Guillain-Barré syndrome, acute sensory ataxic neuropathy, Bickerstaff brainstem encephalitis and pharyngeal-cervical brachial weakness, suggesting that these different clinical presentations are also part of a continuous disease spectrum.

S 3

Common Pitfalls in the Electrodiagnosis of Entrapment Neuropathy

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Carpal tunnel syndrome and ulnar nerve entrapment at the elbow are common entrapment neuropathies. Although these two conditions are commonly seen, and the performance of motor and sensory conduction studies are well described in standard textbooks, the electrodiagnostic evaluation is frequently complex and challenging to even the most experienced electrodiagnostic medicine consultants. A number of the more common pitfalls and its consequences would be discussed.

Idiopathic Intracranial Hypertension

S 4

BL Man
Department of Medicine, Tuen Mun Hospital, Hong Kong SAR

Idiopathic intracranial hypertension (IIH) is defined as increased intracranial pressure without a space-occupying lesion or hydrocephalus and normal cerebrospinal fluid composition. IIH is predominantly seen in women of childbearing age and associated with a history of recent weight gain. It is associated with loss of visual function in up to 25% of cases and progression to blindness if untreated. The incidence of IIH is increasing because of an increased awareness of the syndrome and the increasing prevalence of obesity. The diagnostic evaluation of these patients often involves several medical subspecialties. Coordinating the patient's care from presentation to follow-up is an enormous challenge. This talk offers an updated review of IIH, including epidemiology and pathogenesis, clinical presentations, common clinical course, diagnostic criteria and challenges, and treatments and prognosis.

Atypical Optic Neuritis

S 5

Carmen KM Chan, Andy CO Cheng
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Typically we associate optic neuritis with retrobulbar, demyelinating optic neuritis, which occurs in young females. It may be associated with multiple sclerosis, and it usually improves spontaneously with no treatment. Whilst this scenario may be true in the Caucasian population, it is not infrequent that we encounter 'atypical' optic neuritis in the Chinese population. If we manage 'atypical' optic neuritis like typical ones, we may miss the important therapeutic window.

In this talk we will cover the differential diagnoses, causes and management of atypical optic neuritis, and conditions which can mimic optic neuritis. There will be particular emphasis on neuromyelitis optica and optic perineuritis.

Using Eye Movements for Topological Diagnosis of Central Disorders

S 6

David S Zee
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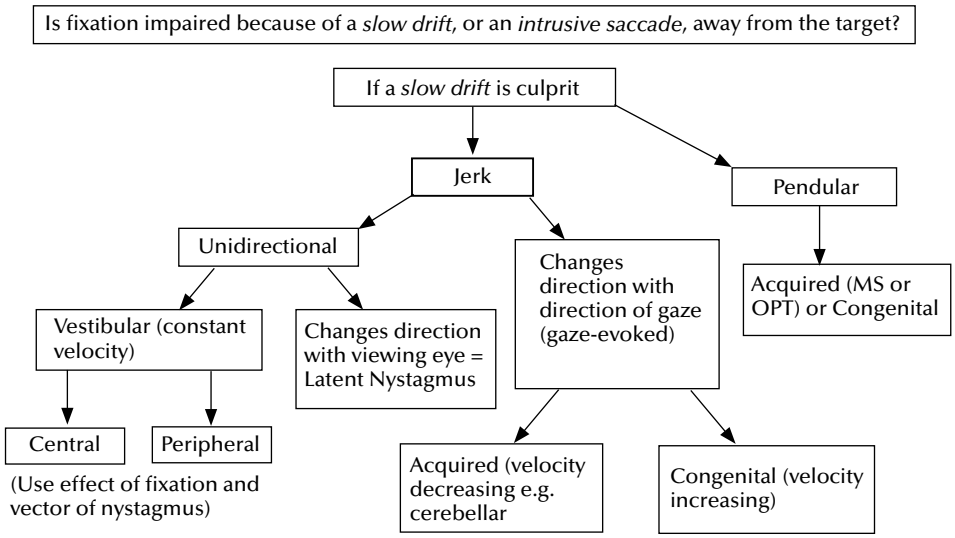
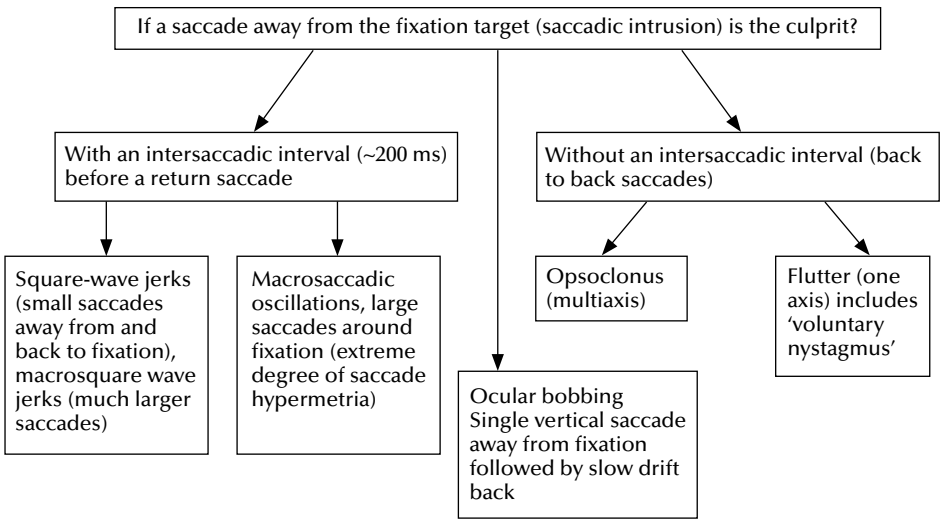
Here we will focus on a careful bedside examination of each of the ocular motor subsystems (saccades, pursuit, vestibular and vergence) to localise and understand our patients' eye movement disorders. We will approach saccade disorders based on abnormalities in initiation, amplitude and speed, and localise them to the cerebrum, brainstem or cerebellum. We will compare midbrain, pontine, medullary and cerebellar lesions and their effects on saccades. Midbrain lesions cause vertical saccade slowing; pontine lesions cause horizontal saccade slowing and medullary and cerebellar lesions cause saccade inaccuracy (dysmetria). Cerebellar vermal lesions cause saccade hypometria and deep cerebellar fastigial nuclei lesions cause saccade hypermetria. Disorders of saccade initiation reflect higher level lesions in the cerebral hemispheres. Pursuit disorders are harder to localise but cerebral hemisphere lesions produce ipsilateral smooth pursuit deficits and contralateral saccade initiation and amplitude deficits. Cerebellar lesions (primarily flocculus and paraflocculus [tonsils]) produce marked pursuit (and eccentric gaze holding) deficits.

We approach nystagmus and other ocular oscillations using a classification based first upon whether the slow phase or the quick phase is the primary abnormality. We will build a decision tree based on which is the primary abnormality.

A Flow Chart For Classification Of Nystagmus



A Flow Chart For Classification Of Nystagmus



New Targets for Treatments of Parkinson's Disease

S 7

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Clinical management of Parkinson's disease involves pharmaceutical interventions and deep brain stimulation. Variable results are found in different patients and there are needs to look for new treatments. Data obtained from laboratories have implicated that there are potential targets to offer neuroprotection to dopaminergic or provide cell replacement of dopaminergic neurons. The present talk will focus on several aspects. Firstly, roles and mechanisms of neurokinins and their receptors, namely NK receptors, will be discussed. Recent results in our laboratory have shown that activation of NK1 receptors is neuroprotective whereas activation of NK3 receptors is detrimental to the survival of dopaminergic neurons. Secondly, roles of N-methyl-D-aspartate receptor (NMDAR) 2B in generation of cell death signalling have been investigated. Gene silencing approach has been employed in reducing the functional expression of NMDAR2B proteins in animals, and these approaches have been found to provide neuroprotective effects to the dopaminergic neurons. Moreover, we have also discovered that there are expressions of reactive astrocytes within an extremely short time window after the onset of Parkinson's disease in animals. The reactive astrocytes express marker of neural stem cells and they are found to release neurotrophic factors which can protect degeneration of dopaminergic neurons and their terminals. Therefore reactive astrocytes are potential cells that can be employed in cell replacement therapy in regenerative medicine. Taking all together, there are potential new targets for Parkinson's disease and some of those could be taken into account for development of new approaches in clinical management of Parkinson's disease.

Acknowledgement
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Levodopa/carbidopa/entacapone as First-line Levodopa Formulation: Pharmacokinetic Considerations

S 8

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Levodopa (LD) is the most efficacious and best tolerated compound for the treatment of patients with Parkinson's disease (PD). This compound is rapidly metabolised in particular by the enzymes aromatic dopa decarboxylase (DD) and catechol-O-methyltransferase (COMT). Inhibition of DD with carbidopa (CD) markedly reduces the peripheral LD degradation. But the short plasma half-life of LD/CD preparations limits its clinical benefit. Therefore, following the LD transport into the brain and the conversion to dopamine, an alternating stimulation of nigrostriatal postsynaptic dopamine receptors takes place. In the long term these fluctuations of dopamine concentrations support onset of motor complications (MC) in PD patients. General opinion is that loss of central compensatory mechanisms of dopamine metabolism is responsible for the development of MC. However, in the periphery, LD troughs are preponderantly associated in clinical practice according to pharmacokinetic investigations with the MC wearing off, which is the reappearance of motor symptoms with decreasing drug effect. A possible strategy to prolong plasma metabolism of LD/CD is the addition of a COMT inhibitor, ie entacapone (EN). Accordingly, combination of the COMT inhibitor EN to LD/CD improved wearing off, since EN prolongs LD half-life and avoids troughs. Pharmacokinetic trials with PD patients also showed that plasma LD peaks are mostly related to the clinical manifestation of the MC dyskinesia, which appear as involuntary movements. One time addition of EN to a LD/CD formulation showed no increase of peripheral maximum LD concentration. But repeat combination of EN to each LD/CD intake elevated plasma LD bioavailability and peaks. Therefore switch from a LD/CD – to a LD/CD/EN regimen may also ask for reduction of LD/CD dosing or delay of the next LD/CD intake, to avoid onset of the most common peak dose dyskinesia. Moreover it may be useful to start with higher dosing of LD formulations in the morning and then to titrate with different LD dosages during the day according to the individual patient's motor behaviour in more advanced stages of PD, as LD plasma availability tends to accumulate during the day with repeated LD dosing. This approach may also prevent onset of dyskinesia. In conclusion, pharmacokinetic studies on peripheral LD metabolism and mode of intake underline their importance as peripheral components for MC manifestations in PD patients. These pharmacokinetic findings in PD patients and healthy volunteers on the impact of COMT-inhibition on LD plasma behaviour may also suggest, that LD/CD/EN as first-line LD formulation may be more appropriate. LD/CD/EN provides less fluctuating LD plasma levels, as shown by pharmacokinetic trials. From the clinical point of view, LD therapy is less complex, when LD/CD/EN is introduced as first-line LD formulation, if tolerated, in PD patients. This approach circumvents the abovementioned COMT-inhibitor related adaption of LD intake following the onset of wearing-off phenomena during repeated LD intake. Such a switch from LD/CD to LD/CD/EN may be complex in particular in more advanced PD patients, as it may ask for a repeated change of LD doses, of number of intakes and of dosing intervals.

Homocysteine and Entacapone Treatment

S 10

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The saga of harmful administration of levodopa (LD) in the treatment of Parkinson's disease (PD) resulted from outcomes of animal, and cell culture studies and the clinical observation of motor complications related to the short plasma half-life of the drug. This discussion did only partially consider a further aspect, which is associated with the long-term administration of LD. Chronic LD intake increases homocysteine levels, which may support progression of the disease due to concomitant onset of neuropsychiatric symptoms and comorbidities, i.e. vascular disease. Homocysteine decrease may therefore be a future therapeutic challenge, which may be achieved by supplementation with certain vitamin or LD/DDI administration with a catechol-O-methyltransferase (COMT) inhibitor. Monitoring of homocysteine may also serve as biomarker for the detoxification potential of endogenous, exogenous and environmental toxins. These substrates may also accumulate in the nervous system, as homocysteine synthesis is associated with O-methylation which has a broad detoxification potential. In the periphery, therapeutic approaches for this LD mediated homocysteine increase are vitamin supplementation, ie folic acid, or application of LD with an inhibitor of COMT. In the brain, a blood brain trespassing precursor of folic acid or a centrally acting COMT inhibitor may represent hypothetical therapeutic approaches. This COMT inhibitor should be applied together with an oxidative stress reducing MAO-B-inhibitor, in order to force central dopamine metabolism further down via the methylation path.

Deep Brain Stimulation for the Treatment of Parkinson's Disease

S 11

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Deep brain stimulation, which involves the implantation of a device that sends electrical impulses to specific targets in the brain, is the surgical treatment of choice when Parkinson's disease (PD) motor complications are inadequately managed with medications. This presentation will discuss the findings of a double-blinded, randomised controlled trial comparing best medical therapy (BMT) and deep brain stimulation (DBS) of the subthalamic nucleus (STN) and globus pallidus (GPi) for the treatment of PD. A total of 255 patients with idiopathic PD were enrolled in Phase I of the study. After 6 months, DBS was more effective than BMT in improving on time without troubling dyskinesia, motor function, and quality of life, but was associated with an increased risk of serious adverse events. In Phase II, 299 patients were randomly assigned to undergo either STN or GPi surgery and stimulation. At 24 months, patients had similar improvement in motor function after either subthalamic or pallidal stimulation. Serious adverse events occurred in 56% of patients undergoing subthalamic stimulation and in 51% of those undergoing pallidal stimulation with no significant between-group differences. The beneficial effects of DBS were sustained over 36 months. Slight declines in some quality-of-life subscales following initial gains and gradual decline in neurocognitive functions likely reflected underlying disease progression and the importance of nonmotor symptoms in determining quality of life. In order to plan a successful DBS treatment, factors including patient selection, target identification, skilled teamwork, post-surgical care and long-term support need to be considered.

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Psychogenic Non-epileptic Seizures

S 12

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Psychogenic non-epileptic seizures (PNES) are found in approximately 25 to 30% of patients admitted to epilepsy monitoring units for seizure diagnosis. Formerly known as pseudoseizures, PNES are events of psychological that alters, or appears to alter, neurologic function in an episodic manner causing transient motor signs, or sensory, autonomic or psychic symptoms, which resemble those occurring during epileptic seizures. PNES are often incorrectly diagnosed for years. This leads to delay in proper treatment, over-utilisation of health care resources, patient anxiety, and potential serious complications from inappropriate medical treatments. Older reports claim many PNES patients also have epileptic seizures, but I and others have found approximately 10% overlap.[1] I found 41/52 (79%) were female with a median age of 38 years. Kalogjera-Sackellares describes two major psychological mechanisms for PNES: (I) Post-traumatic pseudoseizure syndrome in which PNES develop due to one/several traumatic experiences that the patient cannot adequately process or integrate given his/her own psychological resources, and (II) Developmental pseudoseizure syndrome . In the first category, the trauma can be sexual, minor physical, parental, major physical or so-called chronic traumatic life course. Experienced electroencephalographers identify PNES using clinical semiology. Features suggestive of PNES include non-physiologic or non-anatomic progression of signs, out-of-phase body movements, closed eyes, the presence of stuffed animals in adults with normal intelligence, stuttering,[2] inappropriate emotions, and others.

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Upcoming Antiepileptic Drugs: the United States Experience

S 13

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Since 1993, the United States Food & Drug Administration (FDA) has approved 15 new antiepileptic drugs (AEDs). The years of approval and the AEDs, in order, are 1993 felbamate, 1994 gabapentin, 1995 lamotrigine, 1996 fosphenytoin, 1997 topiramate and tiagabine, 1999 levetiracetam, 2000 oxcarbazepine and zonisamide, 2005 pregabalin, 2008 lacosamide and rufinamide, 2009 vigabatrin, 2010 ACTH gel, 2011 ezogabine. The use of felbamate is low due to a 1/4000 risk of aplastic anaemia or hepatic failure. Vigabatrin has low usage due to the risk of peripheral visual field loss. Oxcarbazepine is used in monotherapy for focal-onset seizures (FOS). Zonisamide is approved for adjunctive therapy for adults with FOS, but is also used around the world for myoclonic seizures. Tiagabine is a selective GABA reuptake inhibitor (SGRI) used in adjunctive therapy for FOS. Fosphenytoin is the water-soluble pro-drug of phenytoin, for i.v. and i.m. use. Lacosamide, an amino acid, has a novel mechanism of action: it enhances slow inactivation of neuronal sodium channels. This contrasts with the classic AEDs carbamazepine, lamotrigine, oxcarbazepine, phenytoin, and rufinamide which enhance rapid inactivation of sodium channels. Lacosamide is available in iv and oral forms. It is approved for adjunctive therapy for adults with FOS, but research studies of generalised-onset seizures and children are underway. Rufinamide has some efficacy in FOS, but is FDA approved only for Lennox-Gastaut syndrome. ACTH (Acthar gel) is approved for epileptic spasms only. AEDs awaiting FDA approval are eslicarbazepine, brivaracetam, perampanel and others.

Sleep and Epilepsy

S 14

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Brain activity during sleep is very different from that seen during wakefulness. During non-REM sleep, the brain shows much more synchronised activity than during wakefulness or REM sleep. Sleep disruption is also known to be a risk factor for seizure exacerbation, and many drugs affect sleep, sleep disorders, and seizures. It is therefore not surprising that epilepsy has many potential interactions with sleep and sleep disorders. These include differential diagnosis, timing of certain seizure types, sleep disruption due to seizures, and the frequency and treatment of coexisting sleep disorders.

From a clinical standpoint, both seizures and sleep disorders typically occur outside of a medical setting. They are not witnessed by the treating physician, therefore diagnosis relies heavily on descriptions from patient and onlookers, which can be incomplete at best and misleading at worst. As both parasomnias and nocturnal seizures involve alteration in behaviour and/or consciousness, these can be difficult to distinguish. Prominent examples include nocturnal frontal lobe epilepsy, disorders of arousal, and cataplexy. Thus differential diagnosis of nocturnal seizures therefore often includes sleep disorders, and vice versa.

Certain epilepsy syndromes are profoundly affected by the sleep-wake state. Prominent examples include juvenile myoclonic epilepsy, nocturnal frontal lobe epilepsy, and benign rolandic epilepsy. Some partial seizures also have a relationship with sleep; frontal lobe seizures for example tend to arise more frequently from sleep. These observations can have implications for diagnosis and treatment.

Nocturnal seizures disrupt sleep, even when quite brief. This disruption can be responsible for the difficulty in daytime functioning many patients have following seizures. As sleep disruption can increase the risk of seizures, this can set up a cycle of seizures, consequent sleep disruption, and further intractability of seizures.

Sleep disorders are common in the general population, and many occur even more frequently in patients with epilepsy including insomnia, obstructive sleep apnoea, periodic limb movements, and restless legs syndrome. These are often unrecognised, but when untreated can also contribute to decreased functioning and to intractability of epilepsy.

Most patients with epilepsy take anticonvulsant drugs. These have the potential to alter sleep through improvement in nocturnal seizures; through effects (positive or negative) on coexisting depression, anxiety, or sleep disorders; and through independent effects on sleep.

Quality sleep is known to be important in the consolidation of many kinds of memory, therefore sleep disruption (due to sleep disorders, seizures, or medication) can contribute to the memory problems so often described by people with epilepsy. Vigilance for possible concurrent sleep disorders is important particularly when patients have unexplained somnolence, memory problems, or continued seizures especially if seizures are predominantly nocturnal. Overall, knowledge of the interactions between epilepsy and sleep disorders is essential to the optimal care of patients with epilepsy.

Psychiatric Issues in Epileptic Disorders

S 15

Joyce Lam
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Over the past decades, increasing literatures suggested that epileptic disorder has complex relationships with other neurological, cognitive, psychiatric and behavioural disorders. Epilepsy is now conceptualised as a spectrum condition, as the co-morbid conditions have been demonstrated to share common phenotypes and aetiological factors with epilepsy. Psychiatric illnesses, such as psychosis, and depression, have been demonstrated to be highly prevalent among patients with epilepsy. For example, cross-sectional studies found that the prevalence of depression in patients with epilepsy ranged from 10% to 30% in community-based samples and even mounted up to 50% in clinic populations. Instead of simply a psychological reaction to chronic illness, studies focusing on the temporal associations established that depression is a risk factor for incident unprovoked seizures, suggesting an underlying bi-directional relationship. Psychiatric disorders are also found to share genetic or neurochemical basis with epilepsy. The "iatrogenic" effect, including the use of psychotropics, anticonvulsants and surgical treatment of epilepsy, further complicates the relationships.

This presentation will focus on the psychiatric and cognitive co-morbidities of epileptic disorder, illustrating the clinical epidemiology, aetiological aspects, treatment impact and the co-morbidities in special clinical populations.

Basic Neurogenetics: What Clinical Neurologists Need to Know

S 16

KY Mok
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At bedside, understanding the genetic transmission and the role in pathomechanism is important. It is crucial not only in management of the patient. The importance extends to the care of their family members and may have significant social implication. At macro level, understanding the genetics of disease provide us a view on the pathophysiology.

Syndromes caused by chromosomal insertions and deletions are well documented. Majority of these patients may not be under the care of neurologists. Mendelian or monogenic disorder is probably the most well-known type of genetic mechanism known to clinician but it is not the only one. Many neurodegenerative diseases, eg Parkinson's disease, motor neuron disease have a small portion caused by monogenic disorder. Majority are multi-factorial, ie complex diseases or common disease. This patient group contributes the bulk of clinical load. The apparently same clinical entity can be caused by a single mutation with very large effect size or a multiple of factors with intermediate/small effect size.

Genotype phenotype correlation can be difficult to dissect. Monogenic disorders can have the phenotype altered by other factors. Sex and the special genetic transmission of mitochondria are among these factors. Furthermore, different mutations within the same gene may have different phenotype and mode of inheritance.

It is absolutely true that people from different ethnic origin have more features in common than the difference. There is the other side of the coin, ie difference in disease pattern is no less genuine than the commonality. This is particular important in the approach to genetic disorders, by definition, caused by the genetic makeup of the individual. The differential makeup contributes to the difference in ethnic group and at the same time, the disease spectrum.

Molecular Neurogenetics: Tools and Methods

S 17

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In the post-genomic era, the number of causative genes identified for neurological disorders is increasing in a very rapid pace. These discoveries are accompanied by a proliferation of molecular methodologies that can be applied in a clinical laboratory for accurate detection of mutations in these genes.

The following factors that determine the choice of molecular methods for a particular disease will be discussed.

1. Mutation types: small mutations (eg single base substitutions, small deletions/insertions, splice site mutations, etc), trinucleotide repeats and large mutations (eg exonic or whole gene deletion, large insertion, complex rearrangements)
2. Genetic and allelic heterogeneity
3. Problems specific to mitochondrial DNA

An overview of commonly used molecular methods that are used in clinical laboratories will be presented.

1. Numbering of trinucleotide repeats
2. Mutation scanning versus direct sequencing
3. Methods for detection of large mutations
4. Methods on the horizon: next generation sequencing

Interpretation of molecular findings remains one of the most difficult tasks in genetic testing. Determination of pathogenicity of a novel variant may not be straightforward. Common interpretation problems and potential solutions will be discussed.

Advanced Neurogenetics: Frontiers in Research

S 18

KY Mok
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Recent advances in Parkinson's disease and motor neuron disease will be used as illustration. Discussions will include understanding disease mechanisms based on the study results and practical clinical implications in the new technologies.

Current Approach for Chronic Migraine Management

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Chronic daily headache (CDH) is defined is defined as ≥15 headache days per month for ≥3 months. Chronic migraine (CM) is classified as a disabling complication of migraine without aura by the International Classification of Headache Disorders, 2nd edition (ICHD-2), 2004. It is one subtype of CDH and is defined as ≥15 headache days per month, ≥8 migraine days for ≥3 months in the revised ICHD-2 criteria, 2006. The population prevalence is estimated to be about 1.5 to 2%. It is the common diagnostic entity in headache clinics and many patients with CM overused abortive treatment including ergotamine, triptans, analgesics or narcotics. Emerging evidence suggests that episodic migraine and CM differ, not just in degree, but also in kind. The exact underlying mechanism is not clear but some studies suggest cortical hyper-excitability or dysinhibition. Patients with CM have worse socioeconomic status, reduced health-related quality of life, increased headache-related burden including impairment in occupational, social, and family functioning, and greater psychiatric and medical comorbidities in comparison with episodic migraine.

A detailed history taking and neurological examination are important for the diagnosis of chronic migraine. Secondary headache disorders should be excluded before making the diagnosis. Routine neuroimaging studies are not evidence-based. A headache diary is both helpful for diagnosis and follow-up. Psychiatric comorbidity especially depressive and anxiety disorders are very common in patients with chronic migraine. Psychiatrists should play a major role in the multi-disciplinary treatment team for both psychiatric consultation and treatment. Withdrawal of overused abortive treatment has been suggested for those with medication overuse headache. However, whether prophylactic agents are given at the same time or after withdrawal do not have conclusions.

Patients with CM usually are excluded from migraine prophylaxis trials because they are considered to be too highly disabled and treatment resistant. However, there are a substantial amount of these patients, and indeed, they are the patients who imperatively require effective, safe, and well-tolerated headache prophylactic therapy. Up to now, only onabotulinumtoxinA and topiramate had the best evidence for chronic migraine.

The large trial Phase 3 Research Evaluating Migraine Prophylaxis Therapy (PREEMPT), consisting of two studies (PREEMPT 1 and PREEMPT 2), aims to evaluate the efficacy, safety, and tolerability of onabotulinumtoxinA using a fixed-site, fixed-dose injection protocol (in total 155 U over 31 sites) and an optional addition of 40 U 'follow-the-pain' paradigm. PREEMPT 1 and 2 demonstrated that onabotulinumtoxinA is an effective prophylactic treatment for CM in reducing headache days per month as the primary outcome and most secondary headache symptom measures. Most adverse events (AEs) were mild to moderate in severity, and few patients discontinued the trial (onabotulinumtoxinA, 3.8%; placebo, 1.2%) due to AE. Two randomised controlled studies conducted in the United States and Europe, respectively, demonstrated that topiramate is effective as headache prophylaxis in CM. However, the therapeutic gain of these two treatment agents also was modest despite different study end-points. The moderate effect sizes of these studies pointed out the refractoriness of CM and a potential need of combination therapy in future trials. Of note, both topiramate and onabotulinumtoxinA showed similar efficacy in treatment of CM between those with and without medication overuse.

Updated Guidelines for Treatment of Neuropathic Pain

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Several recommendations regarding the treatment of neuropathic pain have been published in the literature, mostly under the auspices of major professional and academic organisations in North America, Latin America and Europe.[1-6] Overall, there are few differences among the pharmacological recommendations for treating neuropathic pain. In most, tricyclic antidepressants and calcium channel $\alpha 2$-δ ligands are often regarded as first-line therapy, while selective serotonin noradrenaline reuptake inhibitors and topical lignocaine are considered first- or second-line treatments. Tramadol and opioid analgesics are regarded as second- or third-line treatment. A few guidelines suggested combination therapy when monotherapy is unsatisfactory.[5-7]

Despite these guidelines providing evidence-based recommendations for the treatment of neuropathic pain, studies have shown that successful treatments of neuropathic pain at best provide only partial pain relief for about half of those treated.[8] In part, this outcome is due to the limitations in the existing clinical evidence and research in neuropathic pain. Recent recommendations suggest a more rational strategy for the treatment of neuropathic pain, including the following:

(1) careful assessment to establish a diagnosis,
(2) consider the symptoms which may suggest the underlying mechanisms,
(3) identify co-morbidities that affect the treatment,
(4) establish a realistic expectation with patient,
(5) select the appropriate treatment—first-, second-, third-line drugs, avoid drug with significant adverse effects, consider drug that will also improve other comorbidities, eg sleep and mood,
(6) measure functional and HRQOL outcomes other than pain,
(7) reassess the patient after trial period of therapy,
(8) consider combination treatment if monotherapy failed,
(9) refer to pain specialists if therapy failed and if multidisciplinary management is deemed necessary. Other newer treatment options are also discussed in the lecture.

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Trigeminal Autonomic Cephalalgias

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Trigeminal autonomic cephalalgias (TACs) are a group of primary headache disorders characterised by unilateral trigeminal distribution pain in association with ipsilateral cranial autonomic features. TACs include cluster headache, paroxysmal hemicrania and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT syndrome), which are all short-lasting headaches. These short-lasting headaches with autonomic features are characterised by a nexus of activation between trigeminal afferents (giving rise to pain) and cranial parasympathetic efferents (giving rise to autonomic features). In 1997, Goadsby and Lipton first proposed that these headaches should be classified together as a linked pathophysiology is the hallmark of these syndromes and suggested the term trigeminal-autonomic cephalgias (TACs) though it does not imply all these headaches have a common pathogenesis. Their proposal was adopted by the International Headache Society. The headaches are grouped into Chapter 3 of the 2nd edition of International Classification of Headache Disorders (ICHD-II). The nosology of hemicrania continua is unclear and is placed in the Chapter 4 of the ICHD-II. It has a continuous pain with exacerbation that can include cranial autonomic symptoms as part of the phenotype.

Cranial parasympathetic activation (lacrimation, rhinorrhoea, nasal congestion and eye-lid oedema) and sympathetic hypofunction (ptosis and miosis) are the signature features of all TACs and hemicrania continua. Despite their similarities, these disorders differ in their clinical manifestations and response to therapy, thus it is important to recognise them. The importance of diagnosing these syndromes resides in their excellent but highly selective response to treatment. Trigeminal-autonomic reflex is believed to be implicated in the pathophysiology of TACs and it has been shown in animal experiments that stimulation of trigeminal efferents can result in cranial autonomic outflow. PET and functional MRI studies have demonstrated ipsilateral hypothalamic activation in cluster headache and SUNCT syndrome, suggesting an important role of hypothalamic abnormality in these two TACs. The implication of hypothalamus in pathogenesis of TACs is further supported by the success of treatment with hypothalamic stimulation in patients with drug-resistant chronic cluster headache.

In the past few years, many cases of secondary TAC or TAC-like syndrome have been added in the literature. There are no 'typical' warning signs or symptoms. Neuroimaging should be considered in all patients with TAC or TAC-like syndromes before making the diagnosis of a primary headache.

Anticoagulation for Prevention of Stroke in Patients with Atrial Fibrillation

S 22

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Atrial fibrillation (AF) is the most common cardiac rhythm disorder. Compared with the general population, people with AF have a 5-fold increased risk of stroke. Aspirin and vitamin K antagonists (VKAs) are used for prevention of AF-related stroke. Compared to placebo, aspirin reduces the stroke risk by 22%. VKAs reduce the stroke risk by 68% compared to placebo and 52% compared to aspirin. VKAs are therefore currently recommended as first-line therapy in patients with AF and a moderate or high risk for stroke. However, treatment with VKAs is often poorly managed and underused because of several drawbacks. The major drawbacks are unpredictable interactions with food and other drugs, the inconvenience of INR monitoring, the need for dose adjustment, and the perceived risk of bleeding.

Recently, three new novel oral anticoagulants (dabigatran, rivaroxaban, apixaban) were developed. The new oral anticoagulants all share notable advantages over the VKAs, including predictable anticoagulant effects at fixed doses, limited drug and food interactions, no need for routine blood level monitoring, and a broader therapeutic window. Currently, data from four large clinical trials (3 warfarin trials [RE-LY, ROCKET-AF, ARISTOTLE] and 1 aspirin-controlled trials [AVERROS]) on the efficacy and safety of these agents are available.

Dabigatran is a direct thrombin inhibitor and was tested in the RE-LY trial. RE-LY is a randomised non-inferiority study with an open treatment and blinded endpoint assessment. In RE-LY, 18 113 patients who had AF and a risk for stroke were randomised to receive either a fixed dose of 110 or 150 mg dabigatran twice daily or dose-adjusted warfarin (INR 2-3). At a dose of 110 mg twice daily, dabigatran was associated with a similar rate of stroke and systemic embolism to warfarin, and a significantly lower rate of major bleeding than warfarin. At the higher dose of 150 mg twice daily, the rate of stroke and systemic embolism was significantly lower than with warfarin, but the rate of major bleeding was similar to that associated with warfarin.

Rivaroxaban is a direct factor Xa inhibitor and was tested in the ROCKET-AF study. ROCKET-AF is a double-blind non-inferiority study which randomised 14 264 patients with AF who were at increased risk for stroke to receive either rivaroxaban 20 mg once daily or dose-adjusted warfarin (INR 2-3). In the primary analysis, rivaroxaban was associated with a significantly lower rate of stroke and systemic embolism than warfarin. In the intention-to-treat analysis, rivaroxaban was non-inferior to warfarin for prevention of stroke or systemic embolism. The rates of major and non-major clinically relevant bleeding were similar between the groups with a significantly lower rate of intracranial haemorrhage and fatal bleeding in the rivaroxaban group.

Apixaban is an another direct Xa inhibitor and was tested in the AVERROS and ARISTOTLE studies. AVERROS is a randomised double-blind study to investigate the superiority of apixaban 5 mg twice daily compared to aspirin (81-324 mg per day) in 5599 patients with AF and a risk for stroke but are not suitable for or are unwilling to receive VKAs. Apixaban was associated with a significantly lower rate of stroke and systemic embolism and a similar rate of major bleeding compared with aspirin. ARISTOTLE is a double-blind non-inferiority which randomised 18 201 patients with AF and at least one additional risk factor for stroke to receive either apixaban 5 mg twice daily or dose-adjusted warfarin (INR 2-3). The rates of stroke or systemic embolism and major bleeding were significantly lower with apixaban than with warfarin.

It is not appropriate to compare directly the efficacy and safety of the new oral anticoagulants because the study design and the study population were different among the clinical studies. However, the ROCKET-AF study is more exciting to stroke clinicians because 50% of the study population had prior stroke with TIA which means that they are a higher-risk population while the RE-LY study recruited about 20% of their population who had prior stroke with TIA, as did ARISTOTLE and AVERROES. After many years of wrestling with the difficulties of warfarin, it seems quite likely that clinicians now have an embarrassment of riches in new-generation oral anticoagulants for AF.

Surgical Outcomes from Revascularisation Surgery for Moyamoya Disease: Experience in Tuen Mun Hospital, Hong Kong

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Moyamoya disease (MMD) is a rare cerebrovascular disease characterised by stenosis and occlusion of the bilateral internal carotid arteries resulting in the characteristic development of an abnormal network in the areas of the arterial stenosis. Various revascularisation procedures have been used in the treatment of this group of patients. To study the clinical characteristics and long-term outcomes in the treatment of MMD in Hong Kong, we analysed our result at Department of Neurosurgery, Tuen Mun Hospital, Hong Kong.

Data obtained in 23 patients with MMD (mean age 31 years, range 5-64 years) managed in Tuen Mun Hospital between 1995 and 2011 were analysed. Nine of them are in paediatric age range (age <18 years). Nineteen patients presented with acute symptom, three with recurrent transient ischaemic attack (TIA) and one was detected incidentally. Among those with acute presentation, almost half of them (52%) demonstrated acute cerebral haemorrhage in neuroimaging, the rest showed cerebral infarction. Only 17% of these MMD patients showed no cerebral insult in the neuroimaging on presentation. The diagnosis was established clinically and also confirmed by MRI and cerebral angiogram in all patients. Preoperative cerebral angiography showed that the patients are in various stages of disease, but the majority of them (20 out of 38 hemispheres) were in stage 3 of Suzuki classification. Recently we also included CT perfusion study (CTP) with acetazolamine challenge and neuropsychological assessment in our pre-surgical assessment protocol.

Of the 23 patients, 18 received microsurgical revascularisation procedures. Seven patients underwent unilateral and 11 patients bilateral revascularisation (30 treated hemispheres included 1 repeated revascularisation). The surgical procedures included encephaloduroarteriosynangiosis (EDAS) in 15, encephalodurogaleoarteriosynangiosis (EDGAS) in 3, combined EDAS and EDGAS in 9, encephaloduroarteriomyosynangiosis (EDAMS) in 1, Burr hole in 1 and STA-MCA bypass with EDGAS in 1 patient. There was no mortality in our series but we experienced two (6.7%) postoperative cerebral infarction developed out of 30 hemispheres treated. Both of them showed worsen neurology but improved with conservative management.

The mean follow-up period for these 18 patients underwent revascularisation procedure was 75.2 months (range, 1-154 months). Postoperative cerebral angiogram performed showed 90% of frontal graft developed collateral formation achieving grade A or B in Matsushima grading scale (synangiosis more than one-third filling of anterior cerebral artery territory), while 55% of EDAS graft showed similar grading in middle cerebral artery territories. During this follow-up period, one patient developed recurrent haemorrhage 12 years after EDAS procedure. No patient in ischaemic group developed new infarct on revascularised hemisphere in our patient series. Functionally, 66% (12 patients) demonstrated improvement in modified Rankin Scale (mRS) by 1 point or more. The rest of the group showed the same mRS as in preoperative status.

In conclusion, revascularisation surgery in patients with MMD carries a low risk; it is effective at preventing future ischaemic event and improves quality of life.

Surgical Management of Moyamoya Disease

S 24

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Moyamoya disease (MMD) is the most common paediatric cerebrovascular disease of surgical concern.

MMD with symptoms such as TIA, infarction, seizure, headache/orbital pain, haemorrhage is candidate of surgical treatment. For paediatric patients, indirect revascularisation methods, including encephaloduroarteriosynangiosis (EDAS) using superficial temporal or occipital arteries, encephalomyosynangiosis (EMS), encephalogaleo(periosteo)synangiosis (EGS, EGPS), multiple burr hole trephination with insertion of galeoperiosteal flap, and their combination, are recommended. In adult cases, direct revascularisation methods, such as superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis, with/without indirect revascularisation methods, are frequently used. Direct surgery is more useful in adult patients with MMD because the indirect surgery is effective for recruitment of collaterals only in 40 to 50% of adults, in contrast to the paediatric patients who show nearly 100% improvement of CBF if extensive infarction is absent. Direct anastomosis is frequently not feasible in children because of small size and fragility of the vessels.

According to the results of haemodynamic studies, such as cerebral angiography, SPECT, PET and perfusion MRI, the brain areas for revascularisation are selected. Almost always both motor cortex areas are included. We recommend addition of bifrontal EGS/EGPS for revascularisation of anterior cerebral artery (ACA) territories. In some patients with ischaemia in the posterior cerebral artery (PCA) territory, occipital artery is used for EDAS. Some cases of unilateral MMD (probable MMD) are treated with unilateral surgery. Because 25 to 35% of them show progression to the bilateral disease, they should be monitored. Staged operations are designed according to the patient's symptom, haemodynamic data and the rate of disease progression.

Regardless of the surgical method, postoperative good collateral formation is found in 80 to 90% of the patients. Patients with preoperative extensive cerebral infarction show poor collateral formation after surgery.

Perioperative ischaemic complications are not rare. Because of lack of vascular reserve in these patients, they are vulnerable to ischaemia caused by the intraoperative and postoperative hypotension, anaemia, hypovolemia and hypocarbia. Careful preservation of the collateral channels and meticulous monitoring of the haemodynamic factors are essential for the perioperative management of MMD. Most of the postoperative ischaemic complications are evident during the first postoperative week.

In patients with direct revascularisation, sudden increase of perfusion pressure in the ischaemic brain may cause brain damage by temporary hyperperfusion, especially in patients with preoperative prolonged profound ischaemia.

MMD patients younger than 3 years frequently show rapid progression of disease to widespread cerebral infarction. The outcome may be adversely affected by the preoperative bilateral ischaemic damage in this age-group. Even though they are more vulnerable to perioperative ischaemic brain damage than older children, the overall management outcome is better in cases with early surgery.

There is no solid evidence that surgery is beneficial in cases of MMD with haemorrhage, although it has a reasonable theoretical basis. Surgery is frequently recommended for these patients.

Mechanical Thrombectomy in Ischaemic Stroke: a Look at the Toolbox

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Since the introduction of the Merci family of clot retrievers and disruption device, there has been a blossoming in the number of devices designed to re-establish flow in the setting of ischaemic stroke ranging from thrombectomy devices, aspiration devices, stents, and stent-retrievers with many more to come. Efficacy and ease of use are probably the primary determinants of physician utilisation.

This presentation will review the major devices available in North America, Europe and Hong Kong, compare and contrast the mechanisms of action, ease of use characteristics, and review some of the tips and tricks associated with the devices in question.

Review will also include major intra-arterial trials and forthcoming trials that will be of interest in the further development of intra-arterial strategies.

Medical Management of Intracranial Stenosis

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Atherosclerotic stenosis of intracranial large arteries is an important stroke mechanism especially for Asian populations. Intracranial atherosclerosis causes stroke due to the branch occlusion, artery to artery embolism, and both. The intracranial stenosis is not static, and may progress or regress in a relatively short period of time. Progressive stenosis of intracranial arteries is related to the development of ischaemic events.

In Japan, we often use intravenous argatroban, a direct thrombin inhibitor, alone or with antiplatelet agents as acute antithrombotic therapy for atherothrombotic stroke patients with intracranial atherosclerosis. A rationale of argatroban use in acute atherothrombotic stroke is derived from a domestic trial results, but its efficacy for intracranial atherosclerosis is not scientifically established. As another intravenous anticoagulant, the FISS-tris study[1] failed to show a significant benefit of low-molecular-weight heparin over aspirin in patients with acute stroke (<48 h) with large artery occlusive disease (mostly intracranial). For subacute stroke/TIA patients (<90 days) with intracranial artery stenosis, the WASID trial[2] showed higher rates of adverse events and no benefit of warfarin (INR 2.0-3.0) over aspirin. Thus, anticoagulation is not a world-standard strategy for intracranial atherosclerosis.

Dual antiplatelet therapy is a promising choice for intracranial atherosclerosis, although the combination of aspirin and thienopiridine is not routinely recommended for general stroke patients due to increase in bleeding risk. In the CLAIR trial,[3] combination of clopidogrel with aspirin was more effective than aspirin alone in reducing microembolic signals in acute stroke/TIA patients (<7 days) with predominantly intracranial artery stenosis. Progression of M1 or basilar stenosis during 6 months after stroke (<2 weeks) was significantly lower in patients treated with cilostazol plus aspirin than those treated with aspirin alone in the TOSS.[4] Recently, TOSS-2[5] showed similar efficacy of preventing progression of intracranial artery stenosis and new ischaemic lesions between dual therapy using cilostazol and aspirin and the therapy using clopidogrel and aspirin in acute stroke patients (<2 weeks).

Statin, pioglitazone, and some antihypertensive agents are other promising medical option for intracranial atherosclerosis; their therapeutic power should be properly evaluated. Angioplasty and stenting for symptomatic intracranial artery stenosis remains controversial. The recruitment of the SAMMPRIS trial was prematurely terminated because of the higher 30-day stroke and death rates after treatment with intracranial angioplasty combined with stenting using the Gateway-Wingspan system than those after aggressive medical therapy alone.[6] Further studies, and especially studies from Asia, are required to obtain the best therapeutic strategy in patients with intracranial atherosclerosis.

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P 1

Off-label Use of Rituximab in Refractory Neurological Autoimmune Diseases—Experiences of a Regional Teaching Hospital in Hong Kong

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Background: Rituximab is a chimeric mouse-human monoclonal antibody against the protein CD20 which is present on the surface of all B-cell lineages except for the stem cells, pro-B cells and normal plasma cells. Because of the increasing awareness of the role of B-cell in the pathogenesis of various autoimmune neurological diseases, there are increasing off-label prescriptions of rituximab for these serious diseases such as relapsing multiple sclerosis (MS), neuromyelitis optica (NMO) and myasthenia gravis (MG). However, there are no randomised controlled trials in studying these off-label uses of rituximab. We report eight cases where off-label use of rituximab in several refractory neurological conditions at the Prince of Wales Hospital in Hong Kong, a tertiary teaching hospital of The Chinese University of Hong Kong.
Methods: Patients who have received rituximab as an off-label indication were identified from the MS registries, as well as from recall by individual physician who has used it in other conditions such as NMO and MG. Data were retrieved retrospectively from the electronic patient record (ePR) between August 2008 and July 2011. Information including the diagnosis, clinical presentations, concurrent medications and previous treatments, dosages and regimens of rituximab used, side-effects experienced and clinical progress were recorded.
Results: Eight patients received rituximab as off-label use during the period audited. Indications included primary progressive MS, NMO and MG. Two of the cases are male patients. Rituximab was used mainly as maintenance therapy in all cases except in one case in which it was used as an acute induction therapy in one episode. The most common prescribed dosage is 2000 mg per course with regimen of 1000 mg given bi-weekly. Courses of treatment given ranged from 1 to 5, and the time interval between courses ranged from 5 to 11 months. There were no reported serious infusion reaction and no notable adverse events associated with rituximab use during the above audited period.
Conclusions: Overall, the off-label use of rituximab appears to be safe and promising results can be seen in cases of NMO and MG.

P 2

Cisplatin Neuropathy: a Prospective Study on Chinese Patients

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Background: Cisplatin is a frequently used anti-cancer drug, and with inclusion of this drug in combination chemotherapy, high remission rates for different tumours have been achieved. However, its therapeutic use is limited by a dose-dependent and predominantly sensory, peripheral neuropathy.
Methods: In this study, the incidence of this complication was evaluated in 19 Chinese patients treated with cisplatin 120 mg/m^2 every 4 weeks. Patients were excluded if they were over 70 years old, with a history of previous chemotherapy, diabetes mellitus, alcohol abuse, brain and leptomeningeal involvement, AIDS and impaired liver or renal function. The patients were clinically and electrophysiologically tested before and at 3, 6, 9 and 12 months after the initiation of chemotherapy.
Results: None of the 19 patients examined before treatment showed symptoms or signs or electrophysiological evidence of neuropathy. At the cumulative dose of 360 mg/m^2, 12 (63%) out of all the patients developed sensory neuropathy. However, one patient at the cumulative dose of 1080 mg/m^2 had no clinical or electrophysiological evidence of neuropathy whatsoever, whereas at the cumulative dose of 1440 mg/m^2, all the seven survivors developed sensory neuropathy of varying severity. Despite substantial involvement of sensory nerves, there was barely any change in motor nerve conduction. Ototoxicity due to damage of the eighth nerve was detected in eight (42%) patients.
Implications/Conclusions: Cisplatin-induced neuropathy is characterised by a sensory neuropathy. It has been proposed that large myelinated 1a fibres are deranged, probably at the level of dorsal root ganglion cells. Surface recording is preferred to the near needle electrode recording, which has been shown to be more sensitive in detecting SAPs of small amplitude.

P 3

A Lady with Autoimmune Lymphocytic Hypophysitis Presenting with Right 3rd, 4th and 6th Palsies

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A 52-year-old lady with good past health was admitted to hospital in July 2011 because of acute onset of diplopia worst on looking to the left and droopy right eyelid. She did not have headache or other focal neurological symptom. Examination revealed right 3rd, 4th, and 6th palsies. Pupils and visual field (confrontation test) were unremarkable. Other examinations including ENT were normal.

Her RFT, LFT, glucose, CBP, CRP and CXR were normal. ESR was 60 mm/h. CT brain scan revealed a sellar mass (Fig 1). Contrast CTB showed thickened pituitary stalk (0.6 cm), intense homogenously contrast enhancing mass involving the hypothalamus, infundibulum stalk and pituitary gland. Neither erosion of the sellar floor nor abnormal leptomeningeal enhancement was noted. Circle of Willis was normal (Figs 2 and 3).

Immune markers, syphilis serology, tumour markers were negative. Pituitary hormone confirmed panhypopituitarism (including cranial diabetic insipidus and hyperprolactinemia). CSF showed slightly raised protein (0.6 g/L), normal glucose, mildly elevated wbc (8 x 10^6 /l, lymphocyte 90%) but negative Gram's stain, AFB smear, indian ink, culture, cytology, and MTB PCR DNA.

The clinical and radiological findings and laboratory results were highly suggestive of autoimmune lymphocytic hypophysitis (AIH). Intravenous hydrocortisone 100 mg q8h was initiated for secondary hypoadrenalism, followed by 2 weeks of oral prednisolone 60 mg/day and subsequent tapering for AIH. Rapid improvement in cranial nerve palsies was noted within few days. Hydrocortisone, DDAVP and later thyroxine were given. Contrast MRI brain/pituitary 6 days after steroid (Fig 4) showed thickened pituitary stalk (0.4 cm), enlarged pituitary gland with loss of T1 hyperintense signal of posterior pituitary and homogenous contrast enhancement. Features could represent lymphocytic hypophysitis.

The patient was discharged with almost complete neurological recovery. Follow-up assessment and MRI will be performed. Her endocrine state will be monitored.

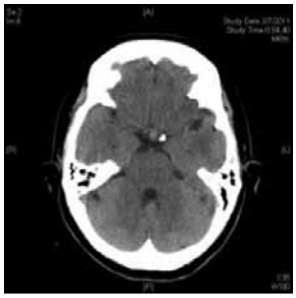

Fig 1. CT brain, plain

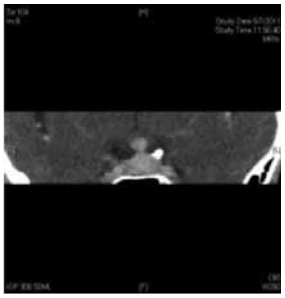

Fig 2. Contrast CT brain (coronal)

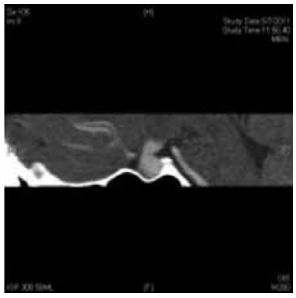

Fig 3. Contrast CT brain (sagittal)

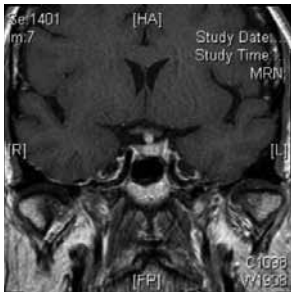

Fig 4. MRI contrast (coronal)

Long-term Outcome of Stroke Thrombolysis in Hong Kong Chinese Patients

P 4

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Background: Emerging data have demonstrated the safety and efficacy of stroke thrombolysis in oriental populations. Long-term benefit was also observed in Caucasian populations. However, data on long-term outcome of Chinese stroke patients who received thrombolysis remain limited.
Methods: Clinical record and stroke registry data of consecutive ischaemic stroke patients received intravenous thrombolysis within 4.5 hours or intra-arterial thrombolysis within 6 hours between January 2007 and August 2010 at our centre were reviewed. Modified Rankin Scale (mRS) scores recorded prospectively at 3 months were compared to that at 12 months and at most recent clinic follow-up.
Results: A total of 60 patients were identified; 42 received intravenous thrombolysis and 18 underwent intra-arterial thrombolysis. The mean age was 71.7 ± 11.8 years and National Institute of Health Stroke Scale score was 16.5 ± 6.7. Twenty-five (42%) patients attained favourable outcome of mRS score ≤2 (ie functional independence) at 3 months. There were 11 (18%) mortality. The proportion of patients (45%) with mRS score ≤2 was sustained at 12 months. Six improved and five worsened between 3 and 12 months. At the most recent follow-up at a mean of 22.5 ± 9.1 months, 19 (32%) patients had deceased but the proportion (42%) with mRS score ≤2 remained static.
Conclusion: The 3-month outcome of stroke thrombolysis in our group of local patients appeared sustainable long term. After 3 months, a small proportion continues to improve in functional status, which was offset by patients who deteriorated or succumbed due to advanced age and comorbidities.

Do Cerebral Microbleeds Increase Intracranial Haemorrhage Risk in Hong Kong Stroke Patients Receiving Thrombolytic Therapy?

P 5

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Background: Cerebral microbleeds (MBs) on T2*-weighted magnetic resonance imaging (MRI) are associated with increased intracranial haemorrhage (ICH) risk. Still, stroke thrombolysis is regarded as safe for patients with MBs as recent Caucasian studies demonstrated small but insignificant increase in ICH risk. We aimed to investigate if thrombolysis is equally safe for local Chinese patients with MBs.
Methods: Consecutive ischaemic stroke patients received intravenous or intra-arterial thrombolysis between January 2007 and June 2011 with MRI performed within 72 hours were recruited. The presence, location, and number of MBs were recorded. Primary outcomes were any ICH and symptomatic ICH by ECASS (European Cooperative Acute Stroke Study) definition.
Results: A total of 54 patients intravenous and 24 intra-arterial thrombolysis patients were identified: 46 of them had MRI performed within 72 hours; 45 were included as one MRI was affected by motion artefact. MBs were detected in nine (20%) patients. Seven had 1 MB, one had 2 MBs, and one had 6 MBs. Nine MBs were subcortical and six were cortical. One (11%) of 9 patients with MBs had asymptomatic ICH at different sites from MB, versus 6 (17%) of 36 patients without (P=1.00). None had symptomatic ICH. For reference, among 33 patients with no or uninterpretable MRI, 10 had ICH of which five were symptomatic.
Conclusion: MBs did not appear to increase ICH risk following stroke thrombolysis in this group of local patients. However, our results should be interpreted with caution as MRI was not uniformly performed. Underestimation of both prevalence of MBs and ICH risk could not be ruled out.

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Intravenous Thrombolysis Versus Intra-arterial Recanalisation Therapy for Acute Ischaemic Stroke Due to Large Artery Occlusion—Comparison of Outcomes from a Hong Kong Hospital

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Background: For ischaemic stroke patients with large artery occlusion and high clot burden, recanalisation rate is low despite intravenous tissue plasminogen activator (IVTPA). Intra-arterial therapy (IAT) has been proposed as an alternative but randomised trial data comparing to IVTPA is lacking. Here we compared the outcomes of our patients treated with either IAT or IVTPA.
Methods: Between January 2007 and May 2011, consecutive patients with large artery occlusion (ICA, MCA M1/M2, VA, BA) treated with IAT, with onset-to-IAT-at-clot time ≤4.5 hours were identified. Favourable outcome was defined as modified Rankin Scale (mRS) score ≤2, and mortality rates at 3 months were compared to patients with large artery occlusion treated with IVTPA at similar time-frame.
Results: Thirteen patients treated with IAT ≤4.5 hours were identified. Mean onset-to-IAT time was 209 ± 38 minutes (range, 150-260 minutes). For comparison, 13 received IVTPA between 2.5 and 4.5 hours (mean 179 ± 19, range 157-230 minutes). There were no statistically significant differences in baseline characteristics of age, NIHSS score and CT-ASPECTS but IVTPA group were treated earlier (P=0.02). At 3 months, 7 (54%) of IAT and 5 (38%) of IVTPA group attained favourable outcome (P=0.69). Mortality rate was 23% in IAT versus 8% in IVTPA group (P=0.59).
Conclusion: No statistically significant differences were found in favourable outcome and mortality rate for our small group of patients treated with IAT or IVTPA. Larger prospective randomised trial is needed to see if IAT is superior to IVTPA for this patient subgroup. In the meantime, IAT should be reserved for patients with contra-indication to IVTPA.

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The Efficacy of Deep Brain Stimulation for Advanced Parkinson's Disease

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Background: Deep brain stimulation (DBS) is a well-established treatment modality for advanced Parkinson's disease (PD) patients whose symptoms are refractory to medical therapy alone. Queen Elizabeth Hospital (QEH) is one of the local public centres which provides this service since July 2000.
Methods: We studied the efficacy of DBS in PD patients over 11 years by record review.
Results: Up to June 2011, 28 patients received DBS in QEH. Subthalamic nucleus was targeted in all but one patients (who received thalamic ventralis intermedius nucleus [Vim] stimulation on one side and STN stimulation on the other). Eleven (39%) were male. The mean (± standard deviation) age of onset and surgery were 43.2 ± 8.9 and 55.2 ± 7.9, respectively. Three patients had already died, two related to disease progression (pneumonia) and one committed suicide by insecticide poisoning (5 years after surgery). We believe one of these patients who died of pneumonia actually suffered from multiple system atrophy, but when he received DBS the classical signs had not yet been manifested (excluded from the remaining analysis).

Baseline and 1-year postoperative Unified Parkinson's Disease Rating Scale (UPDRS) scores were available in 25 and 18 patients respectively, as shown in the following table. The improvements of UPDRS-II and -III were statistically significant.

	UPDRS-I	UPDRS-II	UPDRS-III
Baseline (OFF-med)	4.0 ± 2.7	18.3 ± 6.3	32.7 ± 14.5
One-year post-op (OFF-med, ON-stim)	3.8 ± 1.8	12.3 ± 6.3	16.8 ± 9.1
P value (paired samples T-test)	0.7	0.001	<0.001

Significant reduction of anti-Parkinsonian medications was also achieved (levodopa equivalent daily dose 1090 ± 622 mg to 587 ± 382 mg, P<0.001, paired samples T-test). Ten patients had their implantable pulse generator (IPG) replaced due to battery run-out. The median battery life was 7.1 years (95% confidence interval, 5.1-9.0 years, Kaplan-Meier estimates).
Conclusion: DBS is proven to be efficacious in our cohort. It alleviates symptoms with fewer anti-Parkinsonian medications. Battery longevity is an essential element with a significant impact on the need of IPG replacement and health economy.

A Case with Atypical Neuroleptic Malignant Syndrome

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Case report

A 22-year-old man with mild mental retardation, schizophrenia, anxiety neurosis and epilepsy, receiving quetiapine 350 mg daily and valproate 400 mg BD. The patient was found agitated in workplace, quarrelled with workmates and quitted the job finally. He then experienced unstable mood at home associated with palpitation, diarrhoea and reduced oral intake for recent few days.

He attended Accident Emergency Department (AED) for 5 times within 76 hours and joint consultation with psychiatrists at that time revealed anxious-looking patient with generalised fine tremors. During his 5th AED attendance, he was noted to have a body temperature of 37.5°C. He was given intramuscular injection of 5 mg haloperidol in view of underlying unstable mood and suspected hallucination. He was admitted to medical ward and developed lead-pipe rigidity, mutism, diaphoresis and sialorrhoea. Further drug count discovered patient missing 400 mg of quetiapine and possibility of drug overdose could not be excluded. Vital signs showed normal blood pressure with sinus tachycardia up to 200+ bpm. Temperature raised up to 39°C later the same day of admission with decrease in GCS to E4V1M5. Laboratory investigation showed mild leukocytosis (WBC 16.3 x 10^9 /L) and creatine kinase (CK) level raised up to 2535 IU/L. CT brain and CSF analysis did not reveal any abnormality.

All psychotropic medications were stopped, supportive treatment with bromocriptine, lorazepam and madopar given. Cyproheptadine was empirically started to cover suspected serotonin syndrome. His condition gradually improved and muscle rigidity subsided. CK level peaked at 8080 IU/L on day 7 and later normalised. However, the patient remained mute and transferred to the psychiatric ward for further management.

Discussion

With the common use of atypical neuroleptics, the prevalence of atypical neuroleptic malignant syndrome (which is a milder variant of NMS) is increasing. Our case may be a case of atypical NMS to begin, with subsequent deterioration to typical NMS by the concurrent injection of haloperidol.

Headache Associated with Chest Pain and ECG Abnormalities: What Can It Be?

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Case report

A 60-year-old man, with a history of ischaemic heart disease, was admitted for constricting chest pain and bilateral dull headache. There were mild exertional dyspnoea, dizziness and nausea. Physical examination was unremarkable. ECG showed Q wave in lead III, ST segment depression and T wave inversion in V4-6. It was treated as ischaemic heart disease with antiplatelet. Cardiac enzymes came back normal. Next day morning, he suddenly developed generalised tonic-clonic seizure. Urgent CT brain showed subarachnoid haemorrhage. Cerebral angiogram revealed an elongated aneurysm measuring 2.5 mm x 5 mm in the junction of left A1-A2 and anterior communicating artery. Extraventricular drainage and embolisation of aneurysm were successful but he remained comatose with poor neurological recovery. Severe cerebral oedema secondary to vasospasm developed and he died 5 days later.

Discussion

The diagnosis of cerebral aneurysm was masked by cardiac symptom and ECG changes. It is known that the cardiogenic presentation of SAH spans from ECG abnormalities to elevation of cardiac enzymes and regional wall motion abnormalities. These manifestations are due to the surge of catecholamine release accompanying SAH. ST segment abnormalities were reported in 15 to 51% of SAH and ST depression was more common in patients with poor outcome.

Headache was a predominant symptom in myocardial ischaemia in a number of case reports. In the 2004 International Classification of Headache, the entity "Cardiac cephalalgia" was classified in the group of secondary headaches attributed to disorder of homoeostasis. It could mimic migraine, tension-type headache or other types of headaches that can hardly classified.

This case illustrated two tales in two systems. ECG abnormalities could represent primary changes in myocardial ischaemia or occur secondary to SAH. Headache may be signifying underlying intracranial pathology or solely the predominant manifestation in cardiac cephalgia. Attention should be paid to differentiate the cardiac and neurological causes of headache with ECG changes and neuroimaging should be considered individually.

AUTHOR INDEX

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