E- ABSTRACT BOOK

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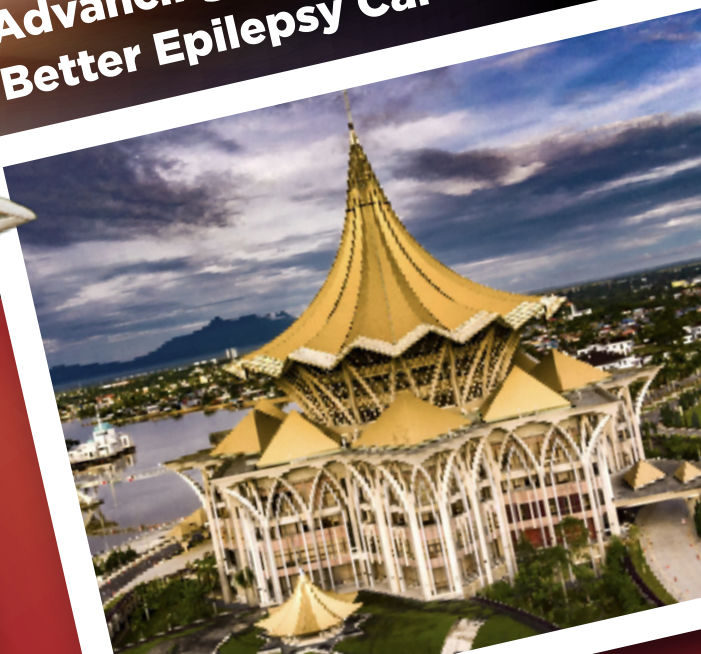

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Adult Neurology
OP-A-01

PREVALENCE OF SEIZURE IN BRAIN TUMORS BASED ON TUMOR LOCATION: A META-ANALYSIS

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INTRODUCTION
The prevalence of seizures in brain tumors commonly associated with tumor location. We aimed to systematically review the literature and identify the relationship between seizure prevalence and tumor location in Gliomas through a meta-analysis.

METHODS
A systematic computerized searches of PubMed, Embase, and Web of Science were performed, searching for studies published up to 01 May 2023. The meta-analysis of pooled prevalence and 95 % confidence interval (CI) for tumor-related seizures were calculated by using a random effect model.

RESULTS
A total of 48 studies that reported seizure prevalence with 18,893 patients were included in this meta-analysis. Overall, Low-grade gliomas have higher pre-operative seizure prevalence compared to high-grade gliomas in all cortical locations, including frontal lobe [LGG: 76% (95 % CI: 68-83 %) vs HGG: 30% (95 % CI: 21-40 %)], temporal lobe [LGG: 77% (95 % CI: 66-87 %) vs HGG 43% (95 % CI: 31-56 %)], parietal lobe [LGG: 75% (95 % CI: 59-89 %) vs HGG 39% (95 % CI: 29-49 %)], and occipital lobe [LGG: 60% (95 % CI: 34-85 %) vs 12% (95% CI: 1-26 %)]. Subcortically located tumors such as insular carries high seizure prevalence as well in low grade gliomas [LGG: 76% (95 % CI: 63-88 %) vs 31% (95 % CI: 16-48 %)].

CONCLUSION
This study discovered the type and grade of brain tumours are the utmost important factors for seizure in brain tumors irrespective of the tumor location.

Adult Neurology
OP-A-02

PREVALENCE OF NEUROLOGICAL SYMPTOMS AND THEIR CORRELATES IN LONG COVID PATIENTS UNDERGOING REHABILITATION

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INTRODUCTION

The post-acute neurologic sequelae of COVID-19 infection has been documented, however there is a lack of data and treatment guidelines for this condition in Malaysia. The study aimed to estimate the prevalence of neurological symptoms and their clinical correlates among recently hospitalised patients diagnosed with Long COVID undergoing outpatient rehabilitation in a single tertiary centre in Malaysia.

METHODS

The study evaluated 2,160 Long COVID patients, referred between November 2020-September 2022, 3-6 months after infection onset. The case definition of Long COVID was based on the World Health Organisation (WHO) Clinical Case Definition Working Group on Post COVID-19 Condition. In-person subject evaluation was conducted by the interdisciplinary rehabilitation team using a standardised multisystem evaluation.

RESULTS

The mean age was 52.7 years (SD 13.4) and 52.3% were males. Neurological symptom prevalence was as follows: Fatigue (66.5%), pain (11.4%), insomnia (7.7%), proximal weakness (7.1%), abnormal sensation (5.9%), psychological dysfunction including anxiety (3.8%), cognitive dysfunction including memory impairment (3.4%), ageusia (1.2%), anosmia (1.0%), neuropathy (1.0%), dizziness (0.6%), and headache (0.2%). The most common non-neurological symptom was dyspnoea (55.9%). Index infection severity (Category 5), organising pneumonia, and pulmonary embolism were weakly correlated with fatigue and proximal weakness (phi coefficient, $\varphi = 0.11\text{-}0.13$, $p < 0.0001$). Fatigue was modestly correlated with dyspnoea ($\varphi = 0.19$, $p < 0.0001$).

CONCLUSION

Fatigue is highly prevalent and underlying respiratory disease may contribute to it. The findings aim to guide the triaging of patients and development of effective rehabilitation guidelines to address the multi-systemic aspects of Long COVID.

Adult Neurology
OP-A-03

ELECTROENCEPHALOGRAM AS A MARKER FOR STROKE SEVERITY

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BACKGROUND
The utility of qualitative electroencephalogram (EEG) as a marker in acute stroke has not been extensively studied. The role of EEG in studying brain function may provide further insights into the effects of stroke. The aim of the study was to correlate the ischemic cortical stroke outcomes with EEG data.

MATERIALS AND METHODS
The cross-sectional study was performed in Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia. EEG data were obtained within 1 week from the onset of stroke symptoms. The inclusion criteria were acute stroke patients who were hospitalized. We excluded stroke mimics such as metabolic or electrolytes derangement, brain infection, cerebral venous thrombosis, traumatic brain injury and drug intoxication. The clinical data and EEG findings were corroborated with the National Institutes of Health Stroke Scale (NIHSS). The abnormal EEG findings were generalized slowing (GS), focal slowing (FS) or epileptiform patterns.

RESULTS
There were 206 participants with a mean age of 64.32 ±12 years old. There were 118 (57.28%) men recruited. The proportion of patients classified according to the stroke severity was as follows: mild (NIHSS 1-4) (85, 41.26%), moderate (NIHSS 5-15) (79, 38.35%), moderate to severe (NIHSS 16-20) (17, 8.25%) and severe (NIHSS 21-42) (25, 13%). The EEG was abnormal in 106 (51.5%) which consists of generalized slowing (39, 18.9%), focal slowing (58, 28.2%) and epileptiform (9,4.4%). There was a significant association between stroke severity and abnormal EEG ($p<0.05$). Epileptiform abnormality had a significant association with stroke severity ($p < 0.05$). Generalized and focal slowing did not show any significant association with stroke severity.

CONCLUSIONS
This study demonstrated that EEG changes such as epileptiform abnormality had a significant association with NIHSS scores. These results indicate that EEG data may be useful to monitor and predict stroke severity.

Adult Neurology
OP-A-04

INTRODUCTION AND VALIDATION OF A NOVEL FOCAL SEIZURE SCREENING TOOL

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INTRODUCTION

A novel focal seizure screening tool was developed (https://doi.org/10.54029/2022xsp) to assist nonneurologists in seizure classification. We aimed to validate this screening tool in real-world practice in the Epilepsy Clinic, University Malaya Medical Centre.

METHODS

A simple and rapid focal seizure screening tool was developed by Schee JP et al. (2022), proposing three categories of symptoms, namely (i) aura (fear, déjà vu, and epigastric aura), (ii) unilateral motor phenomena, and (iii) oral automatism, being significantly associated with the diagnosis of focal seizure. A score of 1 was assigned to each category of symptoms. This self-administered multilingual tool was employed on consecutive patients (or caregivers/eyewitnesses) with confirmed seizure type based on clinical history, neuroimaging, and EEG. Attending clinicians/neurologists subsequently clarified patients' seizure semiology and their scores.

RESULTS*

Among the 125 respondents (68.8% with focal seizures, 31.2% with other seizure types), 92.0% found this tool easy to understand and answer. Their highest education levels were 4.8% primary, 48.0% secondary, and 47.2% tertiary. When a cut-off score of ≥1 was set to identify focal seizure, the tool recorded (i) 96.5% sensitivity, 48.7% specificity, 80.6% positive predictive value (PPV), 86.4% negative predictive value (NPV), positive likelihood ratio (LR+) of 1.88, negative likelihood ratio (LR-) of 0.07, and 81.6% accuracy when scored by respondents, and (ii) 100% sensitivity, 82.1% specificity, 92.5% PPV, 100% NPV, LR+ of 5.57, LR- of 0.00, and 94.4% accuracy when scored by clinicians. Meanwhile, when the cut-off score was ≥2, the tool recorded (i) 65.1% sensitivity, 79.5% specificity, 87.5% PPV, 50.8% NPV, LR+ of 3.17, LR- of 0.44, and 69.6% accuracy when scored by respondents, and (ii) 58.1% sensitivity, 100% specificity, 100% PPV, 52.0% NPV, LR- of 0.42, and 71.2% accuracy when scored by clinicians.

CONCLUSION

This novel, simple and rapid focal seizure screening tool is valid in classifying seizure types.
**Ongoing study with active recruitment. Number of study subjects will be higher by the date of actual presentation. Subsequent phase is a multi-centre project for similar validation process at MOH and MOE centres, followed by assessing the impacts after real-world implementation, specifically improvement in time (i) from first clinic/ED visit to focal seizure diagnosis and (ii) from first clinic/ED visit to targeted ASMs initiation.*

SIGNIFICANCE OF THIS TOOL

1. Easily understood and answered (rapid and simple) upon self-administration, even by patients / caregivers with primary and secondary education levels.
2. When the score is ≥1, it is highly sensitive for focal seizure, hence prompt EEG and MRI for focality are encouraged.
3. When the score is ≥2, it is highly specific for focal seizure, hence early initiation of targeted ASM for focal seizure is encouraged, especially when there is delay in EEG and MRI in resource-limited settings.

OVERALL OBJECTIVES / ENDPOINTS OF THIS PROJECTS

1. Aid general clinicians / non-neurologists in making prompt and accurate focal seizure diagnosis
2. Guide the need for further EEG and MRI assessments for focality
3. Guide the early targeted ASM initiation for focal seizure to improve seizure remission rate

Adult Neurology
OP-A-05

AR IN MEDICAL EDUCATION FOR EPILEPSY CAREGIVERS

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INTRODUCTION

Epilepsy is a chronic neurological disorder that affects millions of people worldwide. Caregivers of epilepsy patients require adequate knowledge and skills to manage seizures effectively. Augmented Reality (AR) technology has the potential to enhance medical education by providing interactive and immersive learning experiences. This study aims to evaluate the effectiveness of an AR-based medical education program for epilepsy caregivers.

METHODS

The study population consisted of a total of 20 epilepsy caregivers who were enrolled in the training course, the caregivers were randomly divided into two groups and then assigned to lecture-based groups and AR-based groups. The learning content included an epilepsy overview, first aid, medication, and safety measures. The effectiveness scores were evaluated using pre/post-knowledge tests, and a satisfaction survey was conducted to assess the participants' experiences.

RESULTS

The total participants' mean pre-test knowledge score was 52±1.67, and the mean post-test knowledge score was lecture-based (68.57±1.16) and AR-based (73.45±1.85), the mean knowledge score of teaching based on AR was higher than that of the lecture group. The difference in the scores between the two groups was not significant. In other words, the training method did not have much effect on the knowledge score of the participants ($P>0.05$). The participants were more satisfied with AR-based education than lecture-based and the difference between the mean scores of satisfaction was statistically significant ($P<0.05$).

CONCLUSION

The study suggests that AR-based training can be the effective and engaging approach to educating epilepsy caregivers. AR-based medical education has the potential to improve knowledge and skills in managing epilepsy. Which can ultimately enhance the safety and quality of life for individuals with epilepsy. Further research should investigate the long-term effects of AR-based training and explore the feasibility of implementing it on a larger scale.

Adult Neurology
OP-A-06

OUTCOME OF HIPPOCAMPAL TAIL RESECTION IN TEMPORAL LOBE EPILEPSY

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INTRODUCTION

Anteromesial temporal lobe (AMTL) resection is commonly performed to treat drug- resistant mesial temporal lobe epilepsy, particularly when secondary to hippocampal sclerosis. Historically, the posterior hippocampus is spared in AMTL resection to minimize language and memory deficits. Recent work has challenged this view by showing that maximal posterior hippocampal resection improves seizure outcome. This study aims to assess if hippocampal tail resection is beneficial for our local patients in improving seizure outcome and subsequently determine whether there is a correlation between volume of residual hippocampus and incidence of seizures.

METHODS

This was a cross-sectional, retrospective study of patients who underwent AMTL resection from 2014 to 2022 in University of Malaya Medical Centre (UMMC). Their details and demographics were extracted from the Electronic Medical Record. Pre-operative and post-operative MRI images were acquired from the UMMC radiology repository. Post-operative MRI was analysed to determine if hippocampal tail was resected. Subsequently, MR volumetry was performed on pre-operative and post-operative MRI using a segmentation software (ITK-SNAP). Volume of the hippocampus and parahippocampal gyrus were measured by a radiologist. Presence or absence of sclerosis in the resected tissue was obtained from the histopathology result verified by a pathologist. Engel classification was used to determine postoperative seizure outcome and all results were statistically analysed for significance.

RESULTS (INTERIM)

35 patients underwent AMTL resection.
All showed hippocampal tail involvement on pre-operative MRI.
10 out of 35 patients had hippocampal tail resection (28.6%).
Percentage of patients achieving Engel class 1 surgical outcome i.e. free of disabling seizures is 70% in the tail resected group whereas in the non-resected group it is 56%.
Correlation between volumetry and seizure control (pending)

CONCLUSION (PRELIMINARY)

Hippocampal tail resection is associated with better post-operative seizure outcome.

Adult Neurology
OP-A-07

SAFETY AND ADVERSE EVENTS FOLLOWING COVID-19 VACCINATION AMONG PEOPLE WITH EPILEPSY: A CROSS-SECTIONAL STUDY

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INTRODUCTION
Epilepsy is estimated to affect 50 million people worldwide. It is known that there is an increased prevalence of morbidity and mortality following COVID-19 infection among people with epilepsy (PWE). However, there is a paucity of information about the adverse events following COVID-19 immunization among them. This study aimed to assess both the safety and adverse events after COVID vaccination among PWE at our hospital, with a focus on the neurologic adverse events following immunization (AEFI).

METHODS
This cross-sectional study recruited 120 adult PWE, who are active patients of the Neurology Clinic, Universiti Kebangsaan Malaysia Medical Centre. Consent-taking was conducted via synchronous or asynchronous approaches, followed by a phone call interview session. The interview collected socio-demographic information, epilepsy-related variables, and vaccination-related variables. Univariate analysis and multiple logistic regression analysis were done to study factors associated with the AEFI of different COVID-19 vaccines.

RESULTS
Among all types of COVID-19 vaccines, most of the PWE received the Cominarty® COVID-19 vaccination (52.5%). Overall, local AEFI was the quickest to develop, with an average onset within a day. PWE with normal body mass index (BMI) were at a higher risk of developing both local and systemic AEFI compared to those underweight and obese PWE. (OR: 15.09, 95% CI 1.70-134.28, p=0.02).

CONCLUSION
COVID-19 vaccines are safe for PWE. AEFI among PWE were similar to those observed in the general population following COVID-19 vaccination. Therefore, clinicians should encourage PWE to be vaccinated against COVID-19.

KEYWORD
Epilepsy, COVID-19 vaccination, adverse events following immunization.

Adult Neurology
OP-A-08

THE EFFECT OF 20-MINUTE MINDFUL BREATHING ON PSYCHOLOGICAL WELL-BEING IN EPILEPSY, A RANDOMIZED CONTROL TRIAL

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ABSTRACT

Background: Depression and anxiety are prevalent among approximately one-third of people with epilepsy (PWE) but not all patients have access to psychiatry or psychological services. Mindfulness-based programs have been well-documented in improving psychological health, however, there were limitations such as time or logistic factors.

OBJECTIVES

This study aimed to determine the effectiveness of the 20-minute mindful breathing, a simpler and shorter intervention, on the psychological well-being of PWE, using an instructional video clip.

METHOD

Twenty adult epilepsy patients who scored ≥ 15 in the Neurological Disorder Depression Index (NDDI-E) or Generalized Anxiety Disorder Scale (GAD-7), which indicates depressive or anxiety symptoms, were recruited and randomized into intervention (n=10), and a waitlist-control group (n=10). The intervention group received a guide to performing a 20-minute mindfulness breathing, and participants in the control group received no intervention during the trial. The participants were assessed at T0: Baseline, T1: 2 weeks after the intervention, and T2: 6 weeks after the intervention, using NDDI-E, GAD-7, and epilepsy-related quality of life (QOILE-31).

RESULTS

The participants in the intervention group showed a significant decrease in depression score (NDDI-E) at T1 (p=.022, partial η^2 = .271) and T2 (p = .056, partial η^2 = .198) as compared to the control group. The anxiety scores in the intervention group had more improvement at T1 than the control group, but the results were insignificant. However, RCI analysis showed improvement in depression (66.67% vs 30.0%) and anxiety score (55.56% vs 20.0%) at T1 but not for T2. The overall score for QOLIE-31 significantly improved in the intervention group but deteriorate in the control group at T1 (p=.036, partial η^2 = .233) and T2 (p=.031, partial η^2 = .244).

CONCLUSION

The 20-minute mindfulness breathing has an immediate effect in decreasing depression and improving the quality of life among people with epilepsy.

Adult Neurology
OP-A-09

QUANTITATIVE ANALYSIS OF NECK MUSCLE T2 RELAXATION TIMES IN CHRONIC MIGRAINE

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INTRODUCTION

Chronic migraine (CM) is commonly associated with neck muscle involvement, which manifests as neck muscle pain, discomfort or tenderness. Neck pain is regarded as a symptom of migraine and often predicts onset of an attack. However, the pathophysiology of neck pain is unclear and neck muscle dysfunction in CM, if any, is poorly understood. Using MR T2 relaxation times (T2 times), we quantified neck muscle activity in CM with and without clinical evidence of neck muscle activation and compared with controls.

METHODS

T2 times of five neck muscles were analysed on 20 CM subjects with neck muscle activation, 20 CM subjects without neck muscle activation and 20 healthy controls. Two circular regions of interest (ROIs) were drawn in mutually exclusive regions within neck muscles on T2 axial images and values averaged at pre-determined levels of each muscle. The natural logarithm of the mean ROI values was computed for echoes 2 to 8 and plotted against echo time. Linear least squares analysis was then used to compute T2 values for each ROI. Headache impact test (HIT-6), neck disability index (NDI) and depression, anxiety, and stress (DASS-21) scores were obtained.

RESULTS

Semispinalis capitis had the longest T2 times (range 47.31-50.44ms), followed by splenius capitis (range 48.71-50.10ms), trapezius (range 46.62-48.99ms), levator scapulae (range 43.49-47.21ms) and sternocleidomastoid (range 40.04-43.00ms). Compared to controls, only T2 times of bilateral splenius capitis and trapezius were significantly higher than controls ($p<0.05$). There was no significant difference in T2 times between migraine subjects with and without neck muscle activation. DASS-21 scores correlated with splenius capitis while NDI correlated significantly with splenius capitis and levator scapulae T2 times ($p<0.05$).

CONCLUSION

Trapezius and splenius capitis were more active in CM. Neck muscles have similar activity in CM subjects regardless of the presence of neck muscle activation. Splenius capitis and levator scapulae activity were positively correlated with DASS-21 and NDI.

Adult Neurology
OP-A-10

ASSOCIATION OF SERUM VITAMIN D LEVEL WITH PERIPHERAL NEUROPATHY IN TYPE 2 DIABETIC PATIENTS ATTENDING IN A TERTIARY CARE HOSPITAL

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INTRODUCTION

Diabetic neuropathy is a long term complication of diabetes that can cause considerable morbidity in many patients leading to a deterioration of their quality of life. Diabetic polyneuropathy is highly prevalent and affects up to 50% of patients with diabetes. A deficiency of vitamin D is common in patients with diabetes and low concentrations are associated with the presence and severity of neuropathy in diabetes. Vitamin D deficiency is shown to be an independent risk factor for diabetic peripheral neuropathy. Aim of the study was to find out the association of serum vitamin D with peripheral neuropathy in type 2 diabetic patients.

METHODS

This cross-sectional analytical study was conducted in the department of Neurology in Mymensingh Medical College Hospital from October, 2017 to September, 2018. A total of 100 type 2 diabetic patients were included after considering inclusion and exclusion criteria, then sample population was divided into two groups, Group –I: Type 2 diabetic patients with peripheral neuropathy. Group –II: Type 2 diabetic patients without peripheral neuropathy.

RESULTS

In this study mean serum vitamin D value of Group-I and Group-II were 15.50±5.08 and 29.33±4.43 ng/ml respectively. The difference was statistically significant ($p < 0.05$). Among the nerve conduction study parameters, in DPN group 82% was sensory motor and 18% was pure sensory and in them mean vitamin D level was 17.16 ± 4.59 and 19.03 ± 7.00 ng/ml respectively. In subgroup analysis 24% was primarily axonal with secondary demyelination, 18% had pure axonal and 8% were pure demyelinating neuropathy and mean value of serum vitamin D level was 16.14 ± 5.29, 17.20 ± 5.40, and 18.25± 3.77 ng/ml respectively.

CONCLUSION

Vitamin D deficiency is associated with diabetic peripheral neuropathy and vitamin D status needs to be monitored in diabetic patients.

Adult Neurology
PP-A-01

FACTORS PREDICTING MODIFIED RANKIN SCORE (mRs) AT 90 DAYS OF INTRAVENOUS THROMBOLYSIS (IVT) IN OLDER ADULTS (≥60 YEARS OLD) PRESENTING WITH ACUTE ISCHEMIC STROKE (AIS) AT HOSPITAL SEBERANG JAYA

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BACKGROUND

It is reasonable to infer that the prevalence of older adults with AIS is rising given that the risk of stroke increases with age especially in in aging countries like Malaysia[1][2]. We aim to look at factors that predict the mRs at 90 days post (IVT) in this subset of patients.

METHODS

All patients aged ≥60 years old who had received intravenous thrombolysis at Hospital Seberang Jaya during the calendar year 2022 for AIS were included. Pertinent information such as age, gender, stroke subtypes (Bamford classification), Charlson Comorbidity Index (CCI), door to needle time, blood pressure and capillary glucose before IVT and mRs at 90 days was retrieved from medical records.

RESULTS

Of the 26 patients reviewed, 10 of them had mRs of 6 at 90 days post AIS. Partial anterior circulation infarct (PACI) was associated with a poorer outcome. ASPECT score <7, higher NIHSS on presentation, longer door to needle time, intracerebral haemorrhage and CCI of ≥5 were factors that herald poor outcome.

CONCLUSION

There are multiple factors that affect mRs at 90 days in older adults with AIS, further analysis is required to recognise these factors and improve outcomes in these patients. It would be worthwhile to look into the cause of death in the patients with mRs 6 in future studies to improve post stroke care.

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Adult Neurology
PP-A-02

DESCRIPTIVE STUDY OF OLDER ADULTS WHO HAD RECEIVED INTRAVENOUS THROMBOLYSIS (IVT) FOR ACUTE ISCHEMIC STROKE (AIS)

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INTRODUCTION

Stroke is one of the most common causes of morbidity and mortality globally, and its prevalence doubles every decade after the age of 55[1][2]. Stroke is Malaysia's third leading cause of death[2]. We aim to describe the characteristics of older adults (age 60 years old and above) who had presented with AIS at Hospital Seberang Jaya (HSJ) and had received IVT for the same in 2022.

METHODS

We included all patients age 60 years old and above who were treated for AIS and received IVT at HSJ during the calendar year 2022. We gathered pertinent information of these patients from the HSJ stroke registry. Data collected included age, gender, NIHSS and ASPECT score on presentation, stroke subtypes as per Bamford criteria, door to needle time (DTN), Charlson Comorbidity Index (CCI), blood pressure (BP) and capillary blood glucose (DXT) prior to administration of intravenous alteplase, modified Rankin score (mRs) at 90 days and 1 year after IVT. In addition to that, we also looked at occurrence of secondary intracerebral haemorrhage (ICH).

RESULTS

Out of the 26 older adults who received IVT, majority were male and were age ≥ 65. Partial anterior circulation infarct (PACI) was the commonest stroke subtype. The age ≥ 65 group had a higher CCI score. The average NIHSS score was 12.6. Among those thrombolysed, 15 of them had ASPECT score above 7. The average DTN was 82.5minutes. Secondary ICH was observed in 5 of them. The average mRs at 90 days and 1 year after IVT was 5 and above in those age ≥ 65 but patients in the 60-64 years old bracket at 90 days and one year had mRs of 3.1 and 3.6 respectively.

CONCLUSION

Those age ≥ 65 with AIS had higher CCI and NIHSS on presentation. This subgroup of patients were also found to have poorer outcome after IVT as the average mRs at 90 days and 1 year was 5 and above. Further analysis to determine the factors that contribute to poorer IVT outcome in this subgroup of patients is needed.

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Adult Neurology
PP-A-03

HEAT STROKE COMPLICATED WITH PANCEREBELLAR DYSFUNCTION: A FORGOTTEN SYNDROME

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INTRODUCTION

Each year, millions of people are exposed to dangers of extreme heat. Heat stroke (HS) is the most serious heat-related illness. We present a case of HS in a healthy young fit man.

METHOD

Case report

19-year-old army recruit suddenly experience dizziness, confusion, and loss of consciousness during his training under extreme weather at ninth of his tenth kilometers training route. He was attended by army paramedic and basic management of wetting and fanning the skin was performed on the spot. He was sent to district hospital for resuscitation. In view of Glasgow Coma Scale score of 3, he was intubated for airway protection. Resuscitation with fluid and inotropic support were carried out. He was subsequently transferred to tertiary hospital for intensive care management. He developed acute kidney injury, hepatic failure, coagulopathy, and rhabdomyolysis. First brain computed tomography shows generalized cerebral edema. Infective markers were negative. Electrocardiography shows sinus rhythm with echocardiogram of ejection fraction 64%, normal ventricular size and valves. In ICU, he was cerebral protected for 48 hours and received 1 cycle continuous veno-venous hemofiltration (CVVH). He was extubated on day 5 and regained full consciousness however clinically noted cerebellar signs of bilateral eyes lateral gaze nystagmus, dysmetria and ataxic gait. Brain magnetic resonance imaging and angiography performed on day 14 shows bilateral cerebellum T1/T2/FLAIR hyperintense signal intensities with restricted diffusion and normal angiography studies. He was further managed with intensive physiotherapy and rehabilitation.

DISCUSSION

HS is a medical emergency with 5% mortality rate. Early recognition and prompt treatment is vital. About 87% HS patient with neurological deficits made full recovery. However, 3% could remain with pancerebellar syndrome.

CONCLUSION

HS can occur to anyone regardless of age and health condition thus it is vital to improve awareness among clinician and public on heat stroke.

Adult Neurology
PP-A-04

ADVERSE EFFECT PROFILE AND ASSOCIATED FACTORS AMONG ADULT WITH EPILEPSY PRESCRIBED WITH ANTISEIZURE MEDICATIONS AT AN AMBULATORY CARE SETTING

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INTRODUCTION
Adverse effects (AE) are the main reason for poor medication adherence and treatment discontinuation that lead to treatment failure with antiseizure medication (ASM). Available data only gather AE symptoms through voluntary reporting by healthcare providers. This study aimed to assess AE and associated factors among adult patients while on ASM under Neuromedical clinic follow-up.

METHODS
All patients prescribed with at least one ASM were screened for eligibility. Samples were randomised using stratified sampling method according to the proportion of ASM utilised. Liverpool Adverse Events Profile (LAEP) was employed to assess AE using assisted self-administered survey. The LAEP score was individually calculated with higher values indicated higher incidence and frequency of AE occurrence. Factors associated with AE based on the LAEP were determined using multiple linear regression analyses.

RESULTS
A total of 105 patients were included for analysis. Of these, 24.8% reported at least 1 AE within the last four weeks since the encounter. The mean score for LAEP was 24.02 (SD ±5.91) with the maximum score of 51. Drowsiness was the most highly reported AE (33.3%), followed by sleep disturbances (31.4%), forgetfulness (29.7%) and shaky hands (19.0%). Multiple linear regression showed older age (β = 0.142, p = 0.002), patients with shorter duration of disease (β = -0.138, p = 0.009), having three or more ASM (β = 2.691, p = 0.048) and had changes in their ASM regimen within the past year (β = 3.304, p = 0.008) were significantly associated with higher LAEP score.

CONCLUSION
Drowsiness was the most common AE reported for ASM. Advancing age, shorter disease duration, having three or more ASM and changes in ASM regimen were all risk factors of acquiring AE with ASM therapy. Recognising these factors may be of benefit in optimizing pharmacotherapeutic management of epilepsy.

Adult Neurology
PP-A-05

THE EFFECT OF GLUTEN SENSITIVITY BASED ON HLA GENOTYPING ON THE DRUG THERAPY OF EPILEPSY

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INTRODUCTION

Gluten sensitivity (GS) is over 2 times more prevalent in patients with epilepsy compared to the general population. It is also known that 99% of people diagnosed with GS were genetically predisposed through the human leukocyte antigen (HLA) HLA-DQ2 and HLA-DQ8. The purpose of this study was to investigate whether underlying GS based on HLA genotyping have an effect on antiseizure medications (ASM) for seizure control.

METHOD

A case-control study was conducted on 50 epileptic patients and 50 normal adults matched for age, gender, and race. Those patients or controls who had gastric or bariatric surgery, treatment for H. pylori, history of antibiotic or steroid or immunomodulating drug use within 4 weeks of enrolment were excluded. The blood samples from both study groups were sent for identifying the presence of one or more of the HLA-DQ alleles (DQ 2.2, DQ 2.5, DQ 7 and DQ 8) further represented by 6 single nucleotide polymorphisms (SNPs), viz. [(i) DQ 2.2 (rs2395182; rs7775228 rs4713586); (ii) DQ 2.5 rs2187668; (iii)DQ 7 (rs4639334) and (iv) DQ 8 (rs7454108)]. Those positive for any one or more of the HLA -DQ genotypes were considered to have GS. The seizure frequency and number and dosage of ASM given to all patients was recorded.

RESULTS

Our study showed that HLA-DQ 2.2 was seen in 9 out of 50 epileptic patients and none in the control group (p: 0.003). However, the prevalence of HLA-DQ 8 was similar in both groups (18 in the epileptic group and 19 in the control group) and the HLA-DQ 2.5 and HLA-DQ 7 were not seen in both groups. Interestingly, 8 epileptics who were positive for both HLA-DQ 2.2 and HLA-DQ 8 (strongly positive) required more than number of ASM for seizure control (p: 0.006).

CONCLUSION

Out of the four HLA-DQ genotypes (HLA-DQ 2.2, DQ 2.5, DQ 7 and DQ 8) indicating the presence of GS in an individual, the strongly positive patients (i.e) HLA-DQ 2.2 and DQ 8 positive required multiple ASM for seizure control. This may suggest a possibility of malabsorption as a factor in the causation of the refractoriness to ASM and a possible benefit from a gluten free diet. Moreover, from this preliminary study we can suggest a HLA genotyping to be routinely tested for those patients requiring multiple ASM.

Adult Neurology
PP-A-06

EARLY STATIN USE AND CLINICAL OUTCOMES IN PATIENTS WITH ACUTE ISCHAEMIC STROKE WHO RECEIVED INTRAVENOUS THROMBOLYSIS: A 10-YEAR FOLLOW-UP

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INTRODUCTION
This study investigated the association between early statin use after stroke and all-cause mortality or 90-day favourable functional outcome (FFO) in thrombolysed patients at Sarawak General Hospital (SGH) over 10 years.

METHODS
We included patients with ischaemic stroke who received thrombolysis at SGH from 2013 to 2022, excluding those who died during hospitalisation or within 14 days after discharge. Data collected covered demographics, risk factors, stroke subtypes and aetiology, NIHSS scores, prior and discharge medications, and intracerebral haemorrhagic (ICH) occurrences. Patients were grouped by the availability of statin in discharge prescriptions. Mortality and 90-day FFO (mRS 0-2) were assessed using Cox-regression and logistic regression models, respectively, adjusting for age, sex, NIHSS, risk factors, stroke subtypes and aetiology, and ICH. Subgroup analyses were conducted for cardioembolic and non-cardioembolic strokes.

RESULTS
A total of 660 patients with ischaemic stroke were included in the study, with 84.5% of them being prescribed statins upon discharge. The statin cohort showed a higher proportion of lacunar strokes and a lower proportion of cardioembolic strokes. Patients who received statin upon discharge demonstrated lower all-cause mortality throughout the follow-up period [median 2.4 (1.0 – 4.5) years], with a hazard ratio (HR) of 0.57 (95% confidence interval (CI): 0.38, 0.85). However, there was no significant odds ratio of 90-day FFO between the two cohorts [odd ratio 1.56 (95%CI 0.83, 3.00)]. Subgroup analyses indicated that among patients with non-cardioembolic strokes, the prescription of statins upon discharge was associated with reduced all-cause mortality [HR 0.52 (95%CI 0.20, 0.91)]. Conversely, among those with cardioembolic strokes, no significant association was observed between statin prescription and all-cause mortality [HR 0.68 (95%CI 0.37, 1.24)].

CONCLUSION
In thrombolysed acute stroke patients, the use of statins was associated with improved mortality outcomes but did not significantly impact functional outcomes. Our findings support the recommendation of prescribing statin in acute stroke upon discharge.

Adult Neurology
PP-A-07

HEALTH-RELATED QUALITY OF LIFE IN MIGRAINE AND NON-MIGRAINE ELDERLY USING EQ-5D VISUAL ANALOG SCALE AND UTILITY INDEX VALUES

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INTRODUCTION

Migraine is a common neurological disorder that affects people of all ages. Healthrelated quality of life (HRQoL) is an important aspect of migraine management, particularly among the elderly population. The EQ-5D is a validated tool for assessing HRQoL, consisting of a visual analog scale (VAS) and a utility index (UI). This study aims to compare HRQoL between elderly individuals with and without migraine using the EQ-5D VAS and UI values.

METHODS

We conducted a cross-sectional study of 186 elderly individuals (age ≥ 65 years) who attended neurology clinics in Tehran between January 2019 and February 2020. Participants were assessed for migraine using the International Classification of Headache Disorders 3rd edition criteria. HRQoL was measured using the EQ-5D VAS and UI values.

RESULTS

Of the 186 participants, 63 had migraine and 126 did not. The mean EQ-5D VAS score was significantly lower in the migraine group compared to the non-migraine group (55.4 vs 67.44, $p < 0.001$). The mean EQ-5D UI score was also significantly lower in the migraine group compared to the non-migraine group (0.36 vs 0.67, $p < 0.001$).

CONCLUSION

Elderly individuals with migraine have significantly lower HRQoL compared to those without migraine. The EQ-5D VAS and UI values provide a valuable tool for assessing HRQoL in elderly patients with migraine, and can help clinicians understand the burden of migraine in this population. Further research is needed to explore effective management strategies for improving HRQoL in elderly individuals with migraine.

Adult Neurology
PP-A-08

APPLICATION OF THE HINTS BEDSIDE EXAM TO DIAGNOSE ACUTE STROKE IN PATIENTS WITH DIZZINESS

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INTRODUCTION

Dizziness is a common presenting symptom in the emergency department. The HINTS exam (Head Impulse, Nystagmus, Test of Skew), a battery of bedside clinical tests, has been shown to have greater sensitivity than neuroimaging in ruling out stroke in patients presenting with acute dizziness. The present study sought to evaluate the diagnostic accuracy of the HINTS bedside examination in diagnosing acute stroke.

METHODS

We conducted a prospective observational study of patients presenting to the emergency department with acute dizziness. Patients who underwent HINTS examination and were diagnosed with either stroke or acute peripheral vestibulopathy were included in the study. We calculated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the HINTS examination in diagnosing stroke.

RESULTS

A total of 80 patients were included in the study, out of which 20 were diagnosed with stroke and 60 with acute peripheral vestibulopathy. The HINTS examination had a sensitivity of 95%, specificity of 98%, PPV of 95%, and NPV of 98% in diagnosing stroke. The Dix-Hallpike maneuver and Romberg test had a sensitivity of 80% and 72%, respectively, and a specificity of 93% and 90%, respectively, in diagnosing acute peripheral vestibulopathy.

CONCLUSION

The HINTS bedside examination is a highly accurate tool for diagnosing stroke in patients presenting with acute dizziness. It has a high sensitivity, specificity, PPV, and NPV, making it a valuable screening tool for clinicians. Rapid and accurate diagnosis of stroke is crucial for timely intervention and improved outcomes. The HINTS examination can aid in the rapid identification of stroke patients, allowing for timely intervention and improved outcomes. Its use should be considered in the evaluation of patients presenting with acute dizziness.

Adult Neurology
PP-A-09

THE PROGRESSION OF QUALITY OF LIFE AMONG EPILEPSY PATIENTS AT UNIVERSITY OF MALAYA MEDICAL CENTRE

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INTRODUCTION

Epilepsy patients are reported to experience a diminished quality of life (QOL). However, the assessment of QOL among epilepsy patients has largely been limited to cross-sectional studies, and there is a scarcity of information regarding their long-term progression. Thus, the objective of this study was to examine the changes in QOL among epilepsy patients at the University of Malaya Medical Centre.

METHODS

A retrospective observational study was conducted involving epilepsy patients in the Neurology clinic at University Malaya Medical Centre. Data were extracted from the database of the Quality of Life in Epilepsy Inventory (QOLIE-31) for 2016, 2017, and 2020. Subjects who completed a minimum of two QOLIE-31 questionnaires were included. The percentage of change in QOLIE-31 score between each year was calculated.

RESULTS

A total of 88 subjects were included in Cohort 1 (2016 vs. 2017) and Cohort 2 (2017 vs. 2020), respectively. Cohort 1 demonstrated a significant improvement in mean scores of QOLIE-31 (57.7 ± 12.2 vs. 63.2 ± 14.2; $p < 0.001$), in terms of seizure worry ($p < 0.001$), emotional well-being ($p = 0.007$), cognitive functioning ($p = 0.004$), medication effects ($p = 0.001$) and social function ($p < 0.001$). However, there was a significant worsening of QOL in Cohort 2 (67.1 ± 15.6 vs. 63.1 ± 14.9; $p = 0.008$), particularly in seizure worry ($p = 0.003$) and cognitive functioning ($p = 0.021$). In terms of percentage of change, Cohort 1 (median = 10.6; IQR = 25.1) demonstrated a significant positive change in mean QOLIE-31 score as compared to Cohort 2 (median = -4.3; IQR = 32.9) ($p < 0.001$).

CONCLUSION

This study provides insights into the progression of quality of life (QOL) among epilepsy patients in Malaysia and highlighted the potential impact of COVID-19 on QOL of epilepsy patients.

Adult Neurology
PP-A-10

ASSESSING CLINICAL OUTCOMES AND QUALITY MEASURE OF THROMBOLYSIS IN PATIENTS WITH ISCHEMIC STROKE AT SARAWAK GENERAL HOSPITAL

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INTRODUCTION
This study presents an analysis of thrombolysis treatment and its associated clinical outcomes over a 10-year period at Sarawak General Hospital (SGH), the sole tertiary referral centre offering this treatment for ischemic stroke in Sarawak.

METHODS
Patients with ischemic stroke who underwent thrombolysis at SGH from 2013 to 2022 were included in the study. We performed descriptive analyses on patient demographics, risk factors, NIHSS scores, prior medications, favourable functional outcome, FFO (modified Rankin Scale, mRS 0-2), mortality and quality measures related to thrombolysis.

RESULTS
A total of 791 ischemic stroke patients received thrombolysis in SGH. The results showed that the majority of the patients were male (60.3%) with a mean age of 61.4 (14.3) years. Hypertension was the most prevalent risk factor for stroke (68.0%), followed by diabetes (33.0%) and atrial fibrillation (29.7%). 3.9% had recurrent stroke and 17.2% were smokers. The study also highlighted the percentages of patients with neurological improvement within 24 hours (51.2%), FFO (mRS 0-2) at discharge, 30 days, and 90 days (55.8%, 48.3% and 47.4%; respectively), as well as mortality rates at 90 days (15.5%) and 1 year (22.7%). Mean onset to door time was 116.5 (65.9) minutes; door to stroke team activation was 25.6 (33.6) minutes and door to CT scan time was 36.1 (75.8) minutes. Mean door to thrombolysis time was 76.9 (42.7) with 41.9% receiving thrombolysis treatment in within 60 minutes on arrival to hospital. Mean onset to thrombolysis time was 192.2 (64.8), with 42.2% of patients receiving thrombolysis treatment within 180 minutes and 8.2% receiving it after 270 minutes.

CONCLUSION
Our study described characteristics, management, and outcomes of thrombolysis in ischaemic stroke patients in Sarawak. Overall, these findings provide essential baseline information to enhance stroke management services and improve thrombolysis treatment in Sarawak.

Adult Neurology
PP-A-11

UNCREDITED INTRAVASCULAR LARGE B CELL LYMPHOMA INVOLVING CENTRAL NERVOUS SYSTEM: A GREAT MASQUERADER

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INTRODUCTION

Intravascular large B-cell lymphoma (IVLBCL) is infrequent and aggressive clinically depicted by an almost exclusive growth of large cells within the lumen of all sized blood vessels. The clinical manifestations are diverse encompassing many nonspecific signs and symptoms such as fever of unknown origin, neurological symptoms and skin lesions.

METHODS

Case report.

RESULTS

We report a case of 49 years old lady with unusual IVLBCL of central nervous system (CNS). She presented with rapidly progressive dementia preceded with seizures and short history of altered sensorium. There were no cutaneous lesions. Plain CT brain showed no significant abnormalities. Cerebrospinal fluid (CSF) analysis was normal except from mildly raised protein. Antinuclear antibody was positive 1: 320 but the remaining autoimmune workup were negative. Electroencephalogram showed cortical dysfunction with occasional sharp wave at right frontoparietal region. Other dementia workups were unremarkable. MRI brain revealed non enhanced biparietal gyri hyperintensities which may represent encephalitis changes. She was empirically treated for viral encephalitis, however, there were still recurrent seizures despite adequate anti-seizure medications with minimal improvement of symptoms. Subsequent admissions noticed bicytopenia with elevated lactate dehydrogenase (LDH). Bone marrow aspirations and trephine biopsy disclosed High Grade Mature B Cell Lymphoma GCB Type. She was subsequently managed by hematology team and started with conventional Rituximab, Cychlophosphamide, Doxorubicin, Vincristine and Prednisolone (R-CHOP) therapy.
Outcomes: Fortunately, she is currently on the road of recovery.

CONCLUSION

High index of suspicion is warranted to diagnose early in order to have a better prognosis.

Adult Neurology
PP-A-12

MILLER-FISHER SYNDROME WITH ACUTE OPHTHALMOPLEGIA : A CASE SERIES

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INTRODUCTION

Miller-Fisher Syndrome (MFS) is a rare neurological disorder characterized by the triad of ophthalmoplegia, ataxia, and areflexia. The presence of anti-GQ1b antibody is most closely associated with acute ophthalmoplegia in MFS [1]. The diagnostic process of MFS can be challenging due to the overlapping clinical features, which can mimic other neurological conditions.

REPORT

We present three cases of MFS who were referred to neurology unit due to acute onset of diplopia. The first patient, a 60-year-old male, who was referred from the ophthalmology clinic to rule out myasthenia gravis. He complained of diplopia and ptosis for one month duration. The second patient, a 69-year-old male, was referred from Emergency Department with history of diplopia, headache and bilateral upper limb numbness lasting for two weeks. The third patient, a 32-year- old male had diplopia and headache for one week duration and was referred from neurosurgery department for evaluation of suspected bilateral abducens nerve palsy. Upon examination, all three patients had complete to near complete ophthalmoplegia as the most prominent feature, with varying degrees of hyporeflexia and mild ataxia. The first patient tested negative for anti-cholinesterase receptor antibody and Repetitive nerve stimulation was normal. All three patients had normal brain imaging, nerve conduction studies, and negative anti-GQ1b antibody.

Follow up of patients after four weeks showed improvement in symptoms including ophthalmoplegia.

CONCLUSION

Though Guillain-Barre Syndrome (GBS) with ophthalmoplegia is strongly linked with a positive anti-GQ1b antibody[2] these cases highlight the importance of diagnosing MFS based on clinical presentation. Subsequent improvement in ophthalmoplegia along with compatible clinical presentation further supports the diagnosis of MFS. Distinguishing MFS from other conditions with worse prognosis and early diagnosis of MFS is vital to ensure appropriate treatment, avoidance of unnecessary investigations, prognostication of the disorder, and initiate timely follow up.

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Adult Neurology
PP-A-13

ASSOCIATION OF SERUM VITAMIN D LEVEL WITH PERIPHERAL NEUROPATHY IN TYPE 2 DIABETIC PATIENTS ATTENDING IN A TERTIARY CARE HOSPITAL

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INTRODUCTION

Diabetic neuropathy is a long term complication of diabetes that can cause considerable morbidity in many patients leading to a deterioration of their quality of life. Diabetic polyneuropathy is highly prevalent and affects up to 50% of patients with diabetes. A deficiency of vitamin D is common in patients with diabetes and low concentrations are associated with the presence and severity of neuropathy in diabetes. Vitamin D deficiency is shown to be an independent risk factor for diabetic peripheral neuropathy. Aim of the study was to find out the association of serum vitamin D with peripheral neuropathy in type 2 diabetic patients.

METHODS

This cross-sectional analytical study was conducted in the department of Neurology in Mymensingh Medical College Hospital from October, 2017 to September, 2018. A total of 100 type 2 diabetic patients were included after considering inclusion and exclusion criteria, then sample population was divided into two groups, Group –I: Type 2 diabetic patients with peripheral neuropathy. Group –II: Type 2 diabetic patients without peripheral neuropathy.

RESULTS

In this study mean serum vitamin D value of Group-I and Group-II were 15.50±5.08 and 29.33±4.43 ng/ml respectively. The difference was statistically significant ($p < 0.05$). Among the nerve conduction study parameters, in DPN group 82% was sensory motor and 18% was pure sensory and in them mean vitamin D level was 17.16 ± 4.59 and 19.03 ± 7.00 ng/ml respectively. In subgroup analysis 24% was primarily axonal with secondary demyelination, 18% had pure axonal and 8% were pure demyelinating neuropathy and mean value of serum vitamin D level was 16.14 ± 5.29, 17.20 ± 5.40, and 18.25± 3.77 ng/ml respectively.

CONCLUSION

Vitamin D deficiency is associated with diabetic peripheral neuropathy and vitamin D status needs to be monitored in diabetic patients.

Adult Neurology
PP-A-14

COLQ-MUTATION CONGENITAL MYASTHENIC SYNDROME WITH OBSTRUCTIVE SLEEP APNOEA AND RESPIRATORY FAILURE

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INTRODUCTION

Congenital Myasthenic Syndromes (CMS) are rare and heterogeneous group of hereditary disorders that impair neuromuscular junction (NMJ) transmission. Mutation in acetylcholinesterase (AChE) collagen-like tail (COLQ) cause CMS with acetylcholine deficiency and end-plate myopathy.

CASE DESCRIPTION

An 18 year old Chinese male, presented with slowly progressive proximal weakness since 9 years old for evaluation. He had normal developmental milestones and has no family history of similar condition. Examination revealed scoliosis, mild facial weakness, proximal limb weakness (shoulder abduction MRC grade 3, elbow flexion 4-, hip flexion 4+) and axial weakness - neck flexion/extension, abdominal muscles (unable to sit up from supine position). His extraocular movement is normal and there was no ptosis.

Creatinine kinase level was normal (88 U/L). NCS are within normal limits. Of note, a characteristic “double hump” CMAP was seen. 3Hz-RNS reviewed significant decremental response consistent with NMJ transmission disorder. Acetylcholine receptor antibody was negative. Genetic testing reviewed compound heterozygous pathogenic variant of COLQ mutation, which causes congenital myasthenic syndrome.

Oral salbutamol was started. Four months later he presented with progressive dyspnea, reduced effort tolerance and excessive daytime sleepiness. ABG showed type 2 respiratory failure; lung function test revealed restrictive defect; polysomnography suggested severe mixed central and obstructive sleep apnoea (AHI 112.8/hr). He was started on CPAP.
Upon latest review, his sleep quality improves, no more daytime sleepiness; muscle weakness remains stable.

DISCUSSION

COLQ-mutation autosomal recessive CMS causes deficiency of acetylcholinesterase. Typical presentation is at birth or infancy. Phenotype described including truncal weakness, proximal limb weakness, scoliosis and respiratory failure. 3Hz RNS typically show decremental response. A characteristic “double hump” CMAP can be seen. Unlike myasthenia gravis and most CMS, treatment with pyridostigmine is not effective but may worsen the condition. Treatment with beta agonist is recommended.

Adult Neurology
PP-A-15

IMMUNE-MEDIATED NECROTIZING MYOPATHY (NAM) RELATED TO SARS-COV-2 INFECTION: A CASE REPORT

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INTRODUCTION

There is a growing body of evidence that severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) or COVID19 infection is associated with the development of autoimmune diseases. A recent systematic review reported that inflammatory myopathies such as immune-mediated necrotizing myopathies may develop during or after COVID19 infection

CASE PRESENTATION

We described a 60-year-old man who was diagnosed with COVID-19 infection and presented later with a two-week history of myalgia, progressive limb weakness, and dysphagia. He had a Creatinine Kinase (CK) level of more than 10,000 U/L and was strongly positive for anti-signal recognition particle (SRP) and anti-Ro52 antibody, and the muscle biopsy revealed paucity-inflammation necrotizing myopathy with necrotic fibers, which was consistent with necrotizing autoimmune myositis (NAM). He responded well clinically and biochemically to intravenous immunoglobulin, steroids, and immunosuppressant Azathioprine

DISCUSSION

COVID-19-related myositis has been reported in up to 10% of infected patients [1]. In a case-control autopsy study, muscle biopsies from 26 of 43 individuals (60%) who had died with a diagnosis of COVID-19 demonstrated signs of muscle inflammation, ranging from mild to severe inflammatory myopathy[2]. There is a very limited literature on autoimmune myositis triggered by COVID-19 infection. A systematic review highlighted nine cases of inflammatory myositis associated with COVID-19 infection, of which two were immune-mediated necrotizing myopathy[3]. (NAM) is a rare subset of idiopathic inflammatory myopathies and manifest acutely over days or weeks, or subacutely over months, causing severe weakness and extremely elevated creatine kinase (CK) levels in the thousands. Histologically, NAM is distinguished from other inflammatory myositis by the presence of necrotic muscle fibers and a lack of inflammation [4] and it has been linked to autoantibodies including anti-signal recognition particle (SRP) and anti-hydroxy-3-methylglutarul-CoA reductase (HMGCR) antibodies (5).

CONCLUSION

In conclusion, SARS-CoV-2 may be associated with late-onset necrotizing myositis and prompt diagnosis and treatment are significantly important to the patient's outcome.

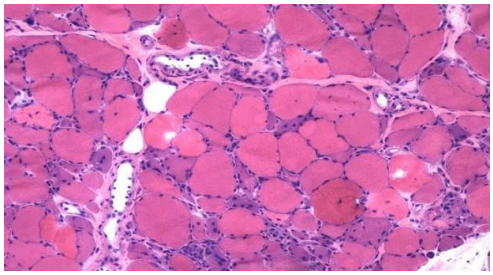

Figure 1a: Muscle pathology showed marked fiber size variation, many necrotizing and regenerating fibers

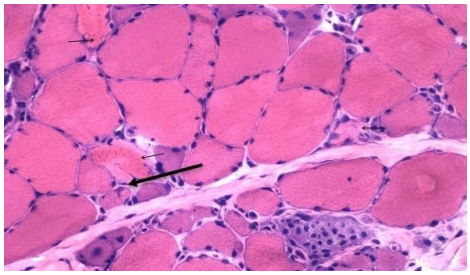

Figure 1b: Necrotic fibres (arrow) are randomly distributed throughout the biopsy and show different stages of necrosis with paleness and coarse feature

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Adult Neurology
PP-A-16

ANTI-RO ANTIBODY MEDIATED NEW ONSET REFRACTORY STATUS EPILEPTICUS

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INTRODUCTION

New onset refractory status epilepticus (NORSE) has been always pose a challenge for clinicians in view of the need for prompt treatment for seizure control along with high probability of poor functional outcome. Although most NORSE cases are remained undiagnosed or cryptogenic, some uncommon causes are also identified.

METHODS

We report a case of a young lady who presented with initial symptoms of high grade fever, subsequently developed refractory super status epilepticus which required up to 5 types of antiepileptic drugs. She was initially treated for viral meningoencephalitis but condition did not improved despite optimal antibiotics treatment. Initial cerebrospinal fluid (CSF) investigations were negative for viral meningoencephalitis PCR screening. Magnetic resonance imaging (MRI) of the brain revealed no abnormalities. Serial EEG showed interictal discharges arising from the right frontal region with severe encephalopathy. Autoimmune screening revealed positive ANA with high titers (1:1280) with positive anti-Ro antibodies. Immunomodulatory treatment were immediately delivered, starting with IV Methylprednisolone & IV Immunoglobulin G. Patient only achieved fit free status after 5th cycle of plasma exchange and followed by 1 cycle of IV Rituximab. Bedside Schirmer's test is abnormal, suggestive of probable Primary Sjogren Syndrome. She is planned for a lip biopsy later for further confirmation.

RESULTS

Neurological manifestations in primary Sjogren syndrome are rare; only a few cases of limbic encephalitis were reported as its initial presentation. In this case, the extensive use of intensive immunotherapy to achieve seizure suppression may reflect the complexity of managing NORSE of this etiology.

CONCLUSION

Anti Ro antibody mediated encephalitis is a rare but treatable cause of NORSE. More awareness needed to recognize and consider neurological presentations of systemic autoimmune rheumatic diseases.

Adult Neurology
PP-A-17

TUMEFACTIVE DEMYELINATING LESIONS VERSUS CNS NEOPLASMS, A 6-YEAR COMPARATIVE STUDY IN MALAYSIA

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INTRODUCTION
Differentiating tumefactive demyelinating lesions (TDL) from neoplasms of the central nervous system continues to be a diagnostic dilemma in many cases.

OBJECTIVE
Our study aimed to examine and contrast the clinical and radiological characteristics of TDL, high-grade gliomas (HGG) and primary CNS lymphoma (CNSL).

METHOD
This was a retrospective, multicentre review of 66 patients (23 TDL, 31 HGG and 12 CNSL) treated between January 2016 and November 2021. Clinical and laboratory data were obtained. MRI brain at presentation were analysed by two independent, blinded neuroradiologists.

RESULTS
Patients with TDLs were younger and predominantly female. Sensorimotor deficits and ataxia were commoner amongst TDL whereas headaches and altered mental status were associated with HGG and CNSL. Compared to HGG and CNSL, MRI characteristics supporting TDL included relatively smaller size, lack of or mild mass effect, incomplete peripheral rim enhancement, absence of central enhancement or restricted diffusion, lack of cortical involvement, and presence of remote white matter lesions on the index scan. Paradoxically, some TDLs may present atypically or radiologically mimic CNS lymphomas.

CONCLUSION
Careful evaluation of clinical and radiological features helps in differentiating TDLs at the first presentation from CNS neoplasms.

Adult Neurology
PP-A-18

A CASE REPORT OF RAPIDLY PROGRESSIVE DEMENTIA WITH PARKINSONISM SECONDARY TO DURAL ARTERIOVENOUS FISTULA

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INTRODUCTION
A dural arteriovenous fistula (dAVF) is an abnormal connection between an artery and vein in the dura matter. It is typically encountered in middle-aged adults with female predominance. Males are likely to display more aggressive neurological symptoms. The presentation can be varied, including increased ICP symptoms, parkinsonism, cognitive decline, and intracerebral hemorrhage.

METHODS
We described a case with right transverse sinus dAVF, presented with parkinsonism and rapidly progressive dementia.

RESULTS
A 66-year-old man, with underlying hypertension, dyslipidemia, glaucoma, and hearing impairment presented with progressive difficulty in walking, swallowing and memory impairment and became bedbound within 3 months. On examination, he has features of Parkinsonism mainly bradykinesia and bilateral limbs cog-wheel rigidity with trunk rigidity and his MMSE was 7/30. Initial MRI Brain showed diffuse symmetrical periventricular white matter T2 hyperintensity mainly at the frontal and parietal lobes suggestive of leukoencephalopathy. Screening of the causes of leukoencephalopathy, including autoimmune, paraneoplastic and thyroid antibodies, were normal. On subsequent review of the MRI brain, diffuse dilatation of cortical blood vessels was noted. MRA and MRV brain with contrast revealed dAVF. A cerebral angiogram confirmed the location of the fistula at the right transverse sinus. He was treated with an embolization and a 3-week intensive rehabilitation. A month later, he could ambulate with a walking stick and his parkinsonism improved. Repeated MRI/MRA/MRV brain with contrast showed resolved right transverse sinus dural arteriovenous fistula and improving venous hypertension changes.

CONCLUSION
Dural AVF should be suspected in patients with parkinsonism and rapid cognitive decline with leukoencephalopathy changes in the MRI brain. Consequently, basal ganglia dysfunction due to impaired drainage of the deep internal veins together with hypoperfusion of the frontal lobes due to venous hypertension may explained the parkinsonism features in this patient. CTA and MRA brain may identify dAVF and allows early intervention.

Adult Neurology
PP-A-19

MIRROR MOVEMENT IN SCHIZENCEPHALY

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INTRODUCTION

We present a case of a 35-year-old man with abnormal movements in his left upper limb (LUL) since early childhood. These movements involuntarily mirrored voluntary movements of his right upper limb (RUL). Independent movement of his LUL was preserved albeit relatively weaker. His first contact with us was in 2021 when he presented with acute tetraplegia. Initial brain CT revealed a hypodense lesion in the posterior aspect of the left lentiform nucleus, along with a right type 2 open-lip schizencephaly.

METHODS

Serial brain CTs were done during index admission. A Brain MRI was performed a year later.

RESULTS

During initial admission, he experienced a tumultuous period that left him severely deconditioned. MRI revealed a T2/FLAIR hyperintense lesion over the left lentiform nucleus extending to the left corona radiata and along the course of the left corticospinal tract down to the visible upper medulla with blooming artefacts on SWI. These were suggestive of a chronic (haemorrhagic) infarct with corticospinal tract degeneration. Additionally, a right frontoparietal open-lip schizencephaly and an absence of a septum pellucidum were appreciated. With intensive rehabilitation, he gradually regained some function in both upper limbs, and his mirror movements ~~features~~ became clinically evident. Unfortunately, he experienced multiple bouts of pneumonia and eventually passed away before further advanced imaging could be conducted.

CONCLUSION

The relative weakness of his LUL may be attributed to the involvement of the right motor area, specifically the hand area of the homunculus, in his right open lip schizencephaly. We also hypothesise that his mirror movements could be a result of functional reorganisation, where the motor cortex of the unaffected hemisphere took on the function of the LUL through projections likely involving the corticospinal tract. This hypothesis is supported by his puzzling tetraplegia following a unilateral stroke. Further advanced imaging would have been beneficial to substantiate these suggestions.

Adult Neurology
PP-A-20

EVALUATION RISK OF NEUROCOGNITIVE IMPAIRMENT WITH A TRANSLATED MALAY LANGUAGE SELF-ADMINISTERED GEROCOGNITIVE EXAMINATION (SAGE) QUESTIONNAIRE IN OBSTRUCTIVE SLEEP DISORDER

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INTRODUCTION

We explore the potential of Self-Administered Gerocognitive Examination (SAGE) questionnaire translated in Malay language as a screening tool to determine the prevalence of neurocognitive amongst Obstructive Sleep Disorder patients and evaluate socio-demographic risk factors.

METHODS

A translated SAGE questionnaire in Malay language (SAGE-ML) was developed and tested for content and face validity and was compared with validated Mini Mental State Examination-Malay Language (MMSE-ML).

À 137 participants with sleep disorder symptoms were recruited from Sleep Clinic Hospital Serdang. Participants were screened with STOP-BANG Questionnaire (SBQ) and were compared with SAGE-ML score.

RESULTS

About 75.2% of participants with screened with SAGE-ML have a normal cognitive function while 12.4% have a mild and a severe neurocognitive impairment respectively. There was a significant association (p =0.000) between severity of sleep disorder with lower SAGE-ML score (cognitive impairment). There was an association between age and SAGE score with elderly have a poor mean rank as compared with young adults. There was no correlation between gender and SAGE score.

CONCLUSION

A significant percentage of patients with sleep symptoms have cognitive impairment elements. A further evaluation to explore the issue is warranted.

Adult Neurology
PP-A-21

BEYOND THE SKIN: UNCOVERING STURGE-WEBER SYNDROME WITHOUT FACIAL ANGIOMATOSIS

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INTRODUCTION

Sturge–Weber syndrome (SWS) is a sporadic neurocutaneous syndrome commonly present with seizure and is characterized by facial port-wine stain and ipsilateral leptomeningeal angioma.

REPORT

16-year-old, male presented with a right-sided partial seizure preceded by a left-sided throbbing headache. No fever, signs of sepsis or meningoencephalitis. He has no previous medical illness and had normal developmental milestones. On general examination, he was disorientated to place and had a right homonymous hemianopia. No facial skin discolouration. His routine blood tests were normal and serum meningitis panel was negative. Non-contrasted CT Brain (Figure 1) showed cortical and subcortical calcification with a 'tram-track' appearance overlying the left parietal lobe. No acute intracranial pathology. MRI Brain (Figure 2) showed changes in keeping with pial angiomatosis without focal ischemia, demyelination or microhemorrhages. The left parietal tram-track calcifications showed no abnormal signals on T1-weighted, T2weighted or gradient-echo (GRE) sequences. Associated ipsilateral frontal sinus and lateral ventricle choroid plexus enlargement noted. Electroencephalography showed left parietal periodic spikes suggestive of ongoing non-convulsive seizure, corresponding to the area of angiomatosis. He was started on sodium valproate and levetiracetam and his confusion and visual field defect subsequently resolved.

DISCUSSION

Five percent of patients with SWS present with leptomeningeal angiomatosis alone, without facial nevus; this is known as type 3 SWS. The encephalofacial angioma in classic SWS is postulated to be a result of failure of the primitive cephalic venous plexus to regress and mature properly in the first trimester of development. A defect involving only the anterior vascular plexus and non-contiguity between the developing vasculature and upper facial ectoderm possibly result in a frontal leptomeningeal angioma without a facial nevus.

CONCLUSION

SWS should be considered as a possible cause of focal seizures, even in the absence of a facial nevus. Specific MRI Brain features aid in its early diagnosis.

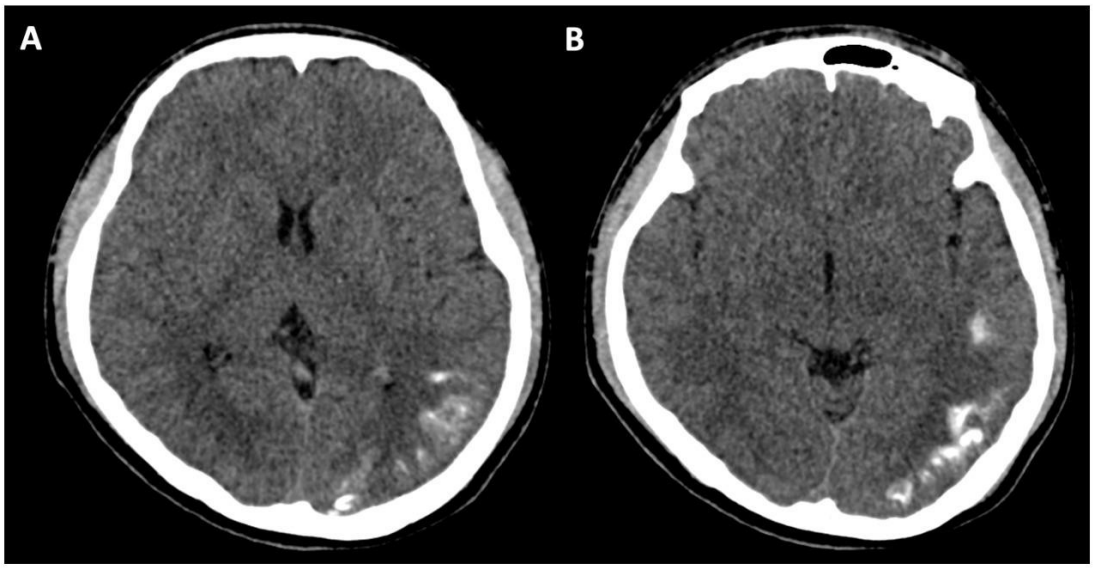

Figure 1. Non-contrasted CT Brain at the level of (A) lateral ventricles and (B) midbrain showing left parietal cortical and subcortical calcification with a 'tram-track' appearance.

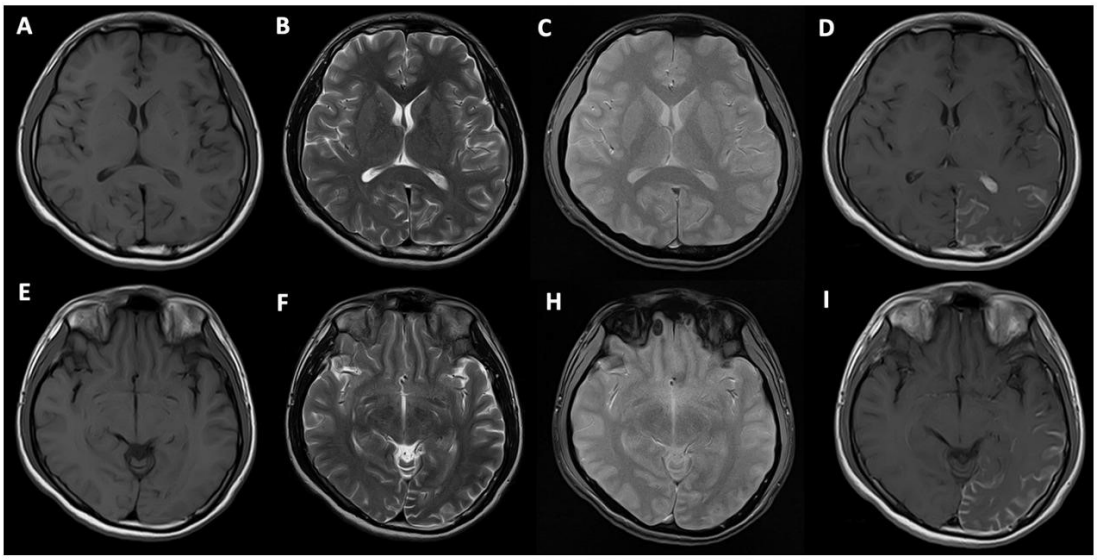

Figure 2. MRI Brain at the level of (A-D) lateral ventricles and (E-I) midbrain in T1-weighted (A, E), T2-weighted (B, F), gradient echo (C, H) and T1-weighted post-contrast sequences showing left parietal pial angiomatosis with no abnormal signals on T1-weighted, T2-weighted and gradient-echo (GRE) sequences corresponding to the tram-track calcifications seen on initial CT.

Adult Neurology
PP-A-22

CLINICAL CHARACTERISTICS OF A RECENT COHORT OF MOTOR NEURON DISEASE PATIENTS IN PENANG ISLAND, MALAYSIA: A RETROSPECTIVE DESCRIPTIVE STUDY

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INTRODUCTION

Motor neuron disease (MND) is a progressive neurodegenerative disorder that affects anterior horn cells. The incidence in South East Asia was 0.40 per 100,000 persons for age standardized rate in 2019. We aim to report the clinical characteristics of MND patients who were diagnosed in the recent two years.

METHODS

Clinical and electrophysiological data were retrospectively extracted from case notes of all newly diagnosed MND patients from 2021-2022 at Neurology Clinic, Penang General Hospital, Malaysia.

RESULTS

A total of ten patients (n=10) were diagnosed with MND from 2021-2022, fulfilling both Gold Coast Criteria and revised El Escorial Criteria. Most patients were Chinese (n=5), followed by Malay (n=3) and Indian (n=2). Male patients were predominant (n=7). Mean age of diagnosis was 57.9 (range: 32 to 76). Mean time from referral to diagnosis was 168.5 days (range: 22 to 426). Of the 10 patients, 9 were amyotrophic lateral sclerosis and 1 was progressive muscular atrophy. 20% (n=2) of the cohort had bulbar onset and a similar proportion could be familial disease. Mean revised-ALSFRS was 38.4 (27 to 45). Half of the patient cohort (n=5) were started on riluzole 50mg BD and the mean time from diagnosis to treatment initiation was 140.6 days (range: 33 to 288).

CONCLUSION

Our cohort showed patient characteristics resembling that of previously reported Malaysian data (male preponderance, age at diagnosis, ethnicity, ALSFRSR score). Diagnostic and treatment delay remain the biggest challenges in our patients.

Adult Neurology
PP-A-23

CEREBRAL VENOUS SINUS THROMBOSIS MANIFESTING AS SPONTANEOUS INTRACEREBRAL HEMORRHAGE: A RARE SEQUELAE OF STREPTOCOCCUS MUTANS INFECTIVE ENDOCARDITIS

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INTRODUCTION

Intracerebral hemorrhage (ICH) in infective endocarditis (IE) is often due to a ruptured mycotic aneurysm or hemorrhagic conversion of cardioembolic stroke, and cerebral venous thrombosis (CVT) is rare in IE. We presented a case of IE complicated by ICH due to CVT.

METHODS

Data regarding clinical presentation, investigation, and treatment were recorded.

RESULTS

A 57-year-old male with underlying rheumatic heart disease was hospitalized for shortness of breath, fever, and lethargy of 1-week. On examination, he was febrile with evidence of Janeway lesions and mitral regurgitation. Diagnosis of mitral valve IE was made based on mitral valve vegetation on echocardiography and positive blood culture which grew Streptococcus mutans. He initially improved after being started on intravenous penicillin and gentamicin however had sudden onset of confusion on the day 12th treatment. Otherwise, he had no signs of meningism or other focal neurological deficits. His blood investigations did not show thrombocytopenia or coagulopathy and he was not on anticoagulant. Since a ruptured cerebral mycotic aneurysm was suspected, CT brain angiography CT (CTA) was performed, which revealed acute ICH in the left frontal, left occipital and left cerebellum with no evidence of aneurysm. A CT venogram showed a filling defect in the left transverse sinus suggestive of thrombosis. A cerebral angiogram revealed superior sagittal sinus and left transverse sinus thrombosis with no evidence of arterio-venous malformation or aneurysm. He had significant resolution of ICH on repeat CT 2 weeks after commencing subcutaneous enoxaparin with a complete return to baseline cognition. He was discharged with apixaban after completing 6 weeks of IV antibiotics and planned for valve replacement.

CONCLUSION

CVT is rare in infective endocarditis but may manifest as ICH and warrants further neuroradiological imaging to distinguish it from a ruptured mycotic aneurysm which management vastly differs from the former.

Adult Neurology
PP-A-24

THE MANY FACES OF TUBERCULOUS MENINGITIS WITH BRAINSTEM INVOLVEMENT IN YOUNG IMMUNOCOMPETENT PATIENTS.

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INTRODUCTION
Tuberculous meningitis (TBM) is an uncommon type of extrapulmonary tuberculosis (TB). One of rare outcome of TBM is immune reconstitution inflammatory syndrome (IRIS). Brainstem involvement is rare, corresponding only to ~5% of CNS tuberculomas.

METHOD
Data from medical records of patients diagnosed with TBM and brainstem involvement at Hospital Universiti Sains Malaysia were retrospectively reviewed. These include clinical features, investigation, imaging findings, and treatments.

RESULTS
Three young immunocompetent patients were included in this case series. The age ranges from 13 to 35 years old. The symptoms include prolonged intermittent fever, headache, seizures and altered behaviour. TB diagnosis was confirmed with a positive CSF Xpert MTB/RIF assay in 2 of the cases, and in the third case via indirect evidence of a strongly positive tuberculin test with supportive clinical features.

All of the patients developed worsening symptoms and the development of new lesions or complications while on anti-TB treatment, including hydrocephalus and increasing tuberculoma sizes in the brainstem. MRI features include contrast-enhanced-rim enhancing lesions at the midbrain in two cases. While the other case shows ill-defined hypodensities at the midbrain and pons. Immune reconstitution inflammatory syndrome in immunocompetent TB (TB-IRIS) was suspected. All patients received anti-tuberculous(TB) treatment, corticosteroid, and CSF diversion procedures.

CONCLUSION
In young immunocompetent patients, treatment of TB meningitis involving the brainstem may not be straightforward due to complication such as obstructive hydrocephalus that developed while the patients are on intensive phase treatment. This may be due to TB-IRIS or deep-seated tuberculoma which requires a longer duration of intensive anti-TB and steroid therapy. Due to the lack of large prospective cohort studies on TB-IRIS in young immunocompetent patients, the diagnosis, and treatment remain a challenge.

Adult Neurology
PP-A-25

A WOBBLY LADY WITH CHRONIC LYMPHOCYTIC INFLAMMATION WITH PONTINE PERIVASCULAR ENHANCEMENT RESPONSIVE TO STEROIDS (CLIPPERS)

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INTRODUCTION

Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) represents a rare central nervous system (CNS) inflammatory disorder which predominantly involves the pons and shows dramatic improvement with steroid.

METHODS

Data from medical records were collected. Clinical features, risk factors, investigations, imaging findings, treatment, and outcomes were recorded.

RESULTS

A 56-year-old lady with underlying hypertension presented with unsteady gait, associated with vertigo and imbalance for 2 month. There was no tinnitus, hearing loss, weakness, numbness, or other cranial nerve symptoms. No raised intracranial pressure symptoms, constitutional symptoms, or any history of stroke or autoimmune disease.

Examination showed severe ataxia with positive cerebellar signs. Systemic examinations were unremarkable. Baseline blood investigations were normal, but she had positive antibody tests for anti-dsDNA 66 IU/ml, Anti RNP/Sm, and Anti PM-Scl 100. Further antibody tests were negative; Anti- Aquaporin 4 receptor, anti-myelin oligodendrocyte glycoprotein (MOG), Autoimmune encephalitis, and paraneoplastic screening.

Brain MRI showed abnormalities in the pons, bilateral middle cerebellar peduncle, and bilateral cerebellar hemisphere. The lesion appears hypointense to isointense on T1, hyperintense on T2 and FLAIR, with curvilinear peppering-like or punctate contrast enhancement patterns, and patchy restricted diffusion in DWI and ADC sequence mainly at the enhanced region.MRS shows a choline peak with reduced N-acetyl-aspartate (NAA) at the enhanced area.

She was given intravenous methylprednisolone 1g OD for 5 days, followed by oral prednisolone 1mg/kg body weight. Her ataxia symptom improved dramatically after 5 days of methylprednisolone.

CONCLUSIONS

CLIPPERS is a newly described pontine-centric inflammatory disorder with distinct clinical and radiological features that can also affect the cerebellar area leading to ataxia. The cardinal feature of the condition is a punctate and/or curvilinear gadolinium enhancement, ‘peppering’ the pons and adjacent hindbrain structures on MRI**.**

Adult Neurology
PP-A-26

DANCING EYES AND FINGERS: POLYMINIMYOCLONUS- A RARE PRESENTATION OF SYRINGOMYELIA

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INTRODUCTION

Polyminimyoclonus is a rare hyperkinetic movement disorder characterized by irregular, multifocal jerky movements of the digits. It has been described to be associated with various neurological conditions including central neurodegenerative disorders, anterior horn cell disease and peripheral nerve hyperexcitability.
We present a case of polyminimyoclonus in a 29-year-old female with Chiari malformation and syringomyelia.

METHODS

Case report

RESULTS

A 29-year-old female presented with a one-year history of oscillopsia and gait instability that had been gradually worsening over the past month.
Clinical examination revealed downbeat nystagmus with a rotatory component and intact ocular movements. Additionally, she exhibited irregular jerky movements of the digits, consistent with polyminimyoclonus. Otherwise, neurological examination showed no abnormalities in tone, power, or sensation. Reflexes were normal. However, she demonstrated clumsiness during tandem gait testing. Routine hematologic and biochemical investigations, including thyroid function, B12 and folate levels were all normal. Nerve conduction studies were unremarkable. Magnetic resonance imaging of the brain and spine was performed, revealing tonsillar descent, indicating Chiari malformation, and a long segment cervicothoracic syringomyelia. Surgical correction of the Chiari malformation and syringomyelia was planned to alleviate symptoms and prevent potential neurological complications.

CONCLUSION

This case highlights the rare association between polyminimyoclonus and syringomyelia. It emphasizes the importance of investigating potential structural abnormalities in patients who present with movement disorders. Further research is needed to elucidate the underlying pathophysiological mechanisms that link these two conditions together.

Adult Neurology
PP-A-27

PROGRESSIVE ENCEPHALOMYELITIS WITH RIGIDITY AND MYOCLONUS (PERM) SECONDARY TO SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A CASE REPORT.

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INTRODUCTION

PERM is characterized by axial and limb rigidity, painful muscle spasms, hyperekplexia, brainstem signs and autonomic dysfunction[1]. PERM can be caused by neoplasia or autoimmune disorders. Here, we report a rare case of PERM secondary to SLE.

CASE DESCRIPTION

A 68-year-old Malay lady who presented with features of parkinsonism symptoms including slowness, rigidity bilateral upper limb and lower limb, forgetfulness, memory loss and slow cognition which gradually worsening for the past 6 months. She also complaints of dysphagia, dysarthria, dizziness, and urinary incontinence. She also has skin tightening and alopecia. She has history of admission 6 months ago for pneumonia with pleural effusion. On examination, the patient has generalized muscle stiffness, myoclonus of the limb and hyperreflexia. She also has skin hyperpigmentation and skin tightening over the face with lip furrowing.

Her CSF analysis showed high protein 0.62g/L (normal 0.15-0.45). We did EMG at rectus femoris, hamstring muscles, abdominal muscles and paraspinal and we noted continuous motor unit activity. We did autoimmune screening, and her ANA and anti dsDNA are positives. MRI showed bilateral hyperintense lesion periventricular region. We were unable to send anti-glycine antibodies (GlyR) and anti-glutamic acid decarboxylase (GAD) antibodies.

She was treated with IV immunoglobulin and IV methylprednisolone. Subsequently, her symptoms showed recovery with absent myoclonus and improved rigidity and stiffness. Then, she began treatment for SLE with iv cyclophosphamide. She was diagnosed with PERM secondary to SLE with central nervous system involvement.

CONCLUSION

The diagnosis of PERM is mainly clinical and can be supported by EMG and antibodies in the serum and CSF. PERM may be associated malignancy and autoimmune disease. In majority of patients, PERM showed good response to immunotherapies, however, relapse can occur.[3] To date, there are no reported cases of SLE presented with PERM and our case showed one rare instances.

Adult Neurology
PP-A-28

A CASE SERIES OF ANTI-SOX1 ANTIBODIES PARANEOPLASTIC NEUROLOGICAL SYNDROME

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INTRODUCTION

Anti-Sry-like high mobility group box (SOX)1 antibodies, also known as antiglial nuclear antibody (AGNA), are specifically found in paraneoplastic neurological syndrome (PNS) and often associated with small cell lung cancer (SCLC). Classical neurological syndromes of anti-Sox1 antibodies are Lambert-Eaton myasthenic syndrome (LEMS) and paraneoplastic cerebellar degeneration (PCD). Due to the rarity of anti-Sox1 antibodies, coexisting onconeuronal antibody and non-neurological manifesting disease, there are knowledge gap on the disease entity. We hereby present a case series of patients with positive anti-Sox1 antibodies.

METHODS

A case series of anti-Sox1 antibodies patients.

RESULTS

Patient 1 was a 66-year-old gentleman who presented with choreiform movement, limbic encephalitis, LEMS and associated with metastatic neuroendocrine carcinoma. Patient 2 was a 25-year-old gentleman who presented with status epilepticus and limbic encephalitis with a possible lung malignancy pending confirmation. Patient 3 was a 69-year-old man who presented with ataxia, encephalopathy, LEMS and associated with papillary carcinoma of thyroid. Patient 4 was a 40-year-old man with underlying acute promyelocytic leukemia presented with parkinsonism syndrome and ataxia. Magnetic Resonance Imaging (MRI) of the brain for anti-Sox1 antibodies is nonspecific and includes symmetrical or unilateral diencephalic, temporal lobes, cerebellar peduncle, brainstem, basal ganglia involvement, and with or without contrast enhancement.

CONCLUSION

Further studies that analyze comprehensive data on anti-SOX1 antibodies are needed.
Our case series presented 4 patients with positive anti-Sox1 antibodies

KEYWORDS

Anti-Sox1 antibodies, paraneoplastic neurological syndrome, Lambert Eaton myasthenic syndrome, lung cancer, neuroendocrine carcinoma

Adult Neurology
PP-A-29

HANAC SYNDROME- AN AUTOIMMUNE MIMIC

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INTRODUCTION

Hereditary angiopathy, nephropathy, aneurysms, and muscle cramps (HANAC) syndrome is a rare genetic autosomal dominant disorder. Primarily, the aetiology is mutations in the COL4A1 gene that encodes the a1 chain of collagen IV located on chromosome 13q34 which is the major component of basement membranes. Hence, blood vessels become much weaker and susceptible to breakage. However, affected individuals may develop intracranial aneurysms which typically do not rupture . Instead, they develop leukoencephalopathy.

CASE REPORT

A 33-year-old lady presented with lower limb weakness associated with spasticity and severe muscle cramps leading to an unsteady gait. She exhibited ophthalmoplegia, diplopia, and dysarthria with features of upper motor neuron lesion on clinical examination. She began experiencing mild memory decline and impaired executive function, which was rather unusual. In the past, she had a history of multiple admissions for acute neuroimmune disorders like Bickerstaff encephalitis and left brachial neuritis. NCS showed mild symmetrical bilateral common peroneal demyelinating neuropathy. The MRI performed revealed nonspecific T2 hyperintensities and microhemorrhages at the subcortical level. Overall, this gives a picture of a combined central and peripheral demyelinating disease. She was treated many times with immunosuppressants such as high dose steroids, intravenous immunoglobulin, and plasma exchange, but to no avail. It is important to suspect a genetic disorder in patients presenting with progressive symptoms and poor response to immune mediated treatments. Genetic testing subsequently revealed a heterozygous likely pathogenic variant in the COL4A1. This is a null variant in which loss of function is a known mechanism of disease.

CONCLUSION

In patients with progressive dyscognition, spastic paraparesis, lower limb cramps, small vessel disease, and microhaemorrhages it is important to consider HANAC syndrome. This would allow appropriate treatment, better outcome, avoid unnecessary procedures, and help in prognosticating the affected individual.

Adult Neurology
PP-A-30

PARRY ROMBERG SYNDROME-AN INTRODUCTION.

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INTRODUCTION

Parry Romberg syndrome, also known as progressive hemifacial atrophy, is a rare and slow progressive unilateral atrophy of facial muscles. Patients are born with a normal morphology of the face where the atrophy begins insidiously at the first two decades of life. This disease tends to stabilize after progressing for a span of 20 years and remains permanent. Although the etiology is said to be unknown, ideas are proposed that this could be related to an inflammatory process associated with chronic vascular disturbance or a neurogenic cause. Commonly affecting the women population, less than 20% eventually develop neurological or disorders.

CASE REPORT

A 45-year-old lady presented with generalized hemifacial atrophy. Until the age of 19, she described her face as normal, evidenced by her pictures. When it first began, she described it as a linear-like lesion on the left forehead and lip and subsequently noted shrinking of the left facial muscles. Over time, the lesion gradually began to progress, causing extensive loss of left hemifacial muscle and fat tissue until it reached a plateau at the age of 25. No family members were experiencing similar symptoms. Clinical examination revealed atrophy of the frontal, orbicularis, temporal, buccal, and area above the upper lip. The classical sign of ‘coup de sabre’, a depressed linear scar extending down through the midface on the left side, resembles a wound made by a sabre can be seen. Rest of the neurological and systemic examinations were normal.

CONCLUSION

Parry Romberg syndrome is a disfiguring disease of an uncertain origin. Diagnosis is solely made based on clinical evidence. Hence, a thorough history and clinical examination are key, as prompt management is essential for optimal quality of life and to prevent further permanent facial deformity. Further research is inevitably required to investigate the root cause of it.

Adult Neurology
PP-A-31

ASEPTIC MENINGITIS WITH IDIOPATHIC INTRACRANIAL HYPERTENSION AS INITIAL PRESENTATION OF SYSTEMIC LUPUS ERYTHEMATOUS

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disorder that affects multiorgan system. The presentation of SLE varies for every patient. The occurrence of neuro-ophthalmic manifestation in SLE is uncommon. We herein report a case of aseptic meningitis with idiopathic intracranial hypertension (IIH) that was later discovered as major SLE.

METHODS

Data regarding clinical presentation, investigation, and treatment were recorded.

RESULTS

A 15-year-old previously healthy girl was admitted for intermittent fever, headache, blurring of vision, and diplopia for two weeks. On examination, she was febrile and there was bilateral cranial nerve VI palsy with papilledema on fundoscopy examination. Laboratory investigation revealed pancytopenia with low complements and raised erythrocyte sedimentation rate. The initial evaluation of autoimmune markers were negative. Plain and contrasted computed tomography (CT) of the brain were normal. Lumbar puncture revealed an opening pressure of > 50 mm H_2O. Cerebrospinal fluid analysis showed elevated cell count with negative cultures. She was treated with intravenous antibiotics. As symptoms of increased ICP persist, repeated lumbar puncture adjunct with oral acetazolamide was commenced and yet she did not show much improvement. Later, she developed prominent facial puffiness with periorbital swelling and non-specific skin rashes. Serial investigation showed persistent low complements with hypoalbuminemia and significant proteinuria. In view of the possibility of SLE diagnosis, we decided to repeat the autoimmune workup and revealed high titre of ANA and dsDNA. Renal biopsy confirmed lupus nephritis class IV. Ultimately, she received high dose corticosteroid, hydroxychloroquine, and completed 6 cycles of cyclophosphamide and now in complete remission with resolution of papilledema.

CONCLUSION

This case highlights the rare neuro-ophthalmic manifestation as presenting features for full-blown SLE and responded well with appropriate treatment. Thus, a high index of suspicion of autoimmune disorder should be considered especially when dealing with young patients with neuro-ophthalmic presentation.

Adult Neurology
PP-A-32

UNMASKING OF CO-EXISTING PATHOLOGIES POST COVID VACCINATION: SERONEGATIVE AUTOIMMUNE ENCEPHALITIS WITH INFLAMMTORY CSF, SCN9A GENETIC MUTATION WITH PROGRESSIVE MYOCLONUS, EPILEPSY AND ATAXIA WITH FOCAL CORTICAL DYSPLASIA

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INTRODUCTION & METHODS (NARRATIVE REVIEW)

We report the case of a previously healthy young Chinese Male without familial history of epilepsy, who presented with new onset focal seizures with loss of awareness, recurrent bouts of refractory status epilepticus requiring intubation and ventilation, myoclonus, opisthotonic posturing, dystonia, and dyscognition post one month of Covid-19 vaccination. CSF results showed inflammatory changes with abundant polymorphs and lymphocytes, mildly raised proteins and normal sugars, negative studies for bacterial, viral or fungal infection. CSF and blood were also negative for all currently commercially available autoantibody markers repeatedly checked at multiple overseas centers.

MRI brain showed isolated right frontal focal cortical dysplasia with cerebral atrophy. He developed symptoms suggestive of autoimmune encephalitis and Progressive Myoclonus Epilepsy (PME), within a month of after receiving his Covid vaccination Genetic studies showed positive heterozygous SCN9A gene mutation. He had multiple admissions for status epilepticus complicated with multiorgan involvement. His symptomatology with relapses and remissions followed the typical sequalae of an autoimmune encephalitis responsive to steroids, iv immunoglobulins, plasma exchange and rituximab. It was also noted the symptoms of seizures and myoclonic jerks were triggered by starvation, infection, and fever such as that seen in SCN9A related epilepsies. Interictal EEGs showed evidence of diffuse encephalopathy with focal epileptiform activity over the right fronto-temporal regions and multiple episodes of ictal electrographic seizures with foci over both fronto-temporal regions. PET scans showed diffuse bitemporal hypometabolism.

CONCLUSION

We strongly believe this rare case highlights real-world evidence of a complicated disease process triggered by complex interaction between post inflammatory changes of Covid-19 vaccination leading to seronegative autoimmune encephalitis in the background of a genetic SCN9A mutation seen in febrile/Dravet syndrome and concomitant structural defect in the brain. Currently the patient is fit free and stable on 4 antiepileptic drugs with dyscognition, ataxia and tube feeding supplementing oral feeds.

Adult Neurology
PP-A-33

OVERLAPPING MYASTHENIA GRAVIS AND MILLER FISHER SYNDROME: A RARE ENTITY

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INTRODUCTION

Miller Fisher syndrome (MFS) is a rare variant of Guillain Barre Syndrome (GBS) which comprises of opthalmoplegia, ataxia and areflexia, accounting of 1-5% of all GBS cases. Co-occurrence of this syndrome with Myasthenia Gravis (MG), another autoimmune disease is very uncommon and can give rise to a challenging clinical diagnostic dilemma.

METHODS

We report a case of a young woman who presented with acute diplopia, dysphagia and unsteady gait for three days with history of preceding upper respiratory tract infection prior to event. Bedside neurological examination showed bilateral ptosis with complex opthalmoplegia, and absence of deep tendon reflexes. Trial of pyridostigmine was given which only yield minimal response. She subsequently developed respiratory distress requiring ventilator support in the Intensive Care Unit (ICU). Her clinical condition improved significantly after one course of Intravenous Immunoglobulin (IVIG). Antibodies against both GQIb and Acetylcholine Receptors turned out to be positive. Computer Tomography (CT) of the Thorax for thymoma surveillance was negative. She was discharged well with pyridostigmine & steroid maintenance therapy along with intensive rehabilitation plan.

RESULTS

Only a few cases of overlapping MG and MFS were reported to date, and most cases had similar neuro-ophthalmic presentation. Clinical diagnosis was only confirmed after series of ancillary investigations. In our case, patient developed Myasthenic Crises and showed good recovery with IVIG treatment.

CONCLUSION

Despite the rare co-occurrence, superimposed conditions of both MG and MFS should be considered in patients with atypical presentation to ensure proper diagnosis and delivery of correct treatment. Further research needed to study the basis and similarities of immunological pathogenesis in both diseases.

Adult Neurology
PP-A-34

IMMUNE MEDIATED ENCEPHALITIS: A CASE OF A REFRACTORY STATUSEPILEPTICUS WITH POSITIVE SYSTEMIC ANTIBODY

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INTRODUCTION

Autoimmune encephalitis can present as a wide variety of symptoms from mild to complex forms of encephalopathy with refractory seizures; making the diagnosis to be very challenging. We report a case of a young lady who presented with refractory status epilepticus and nonspecific autoimmune positive.

CASE DESCRIPTION

A 13 years old girl was admitted twice to our centre for refractory status epilepticus focal motor seizure with impaired awareness. In both cases, she was intubated with recurrent episodes of focal motor seizure despite being given immunoglobulin and multiple anti-epileptic drugs. She was first presented with stiffness of her right upper limb and right facial twitching with head and eye eversion. Her CSF culture analysis was within normal parameter and negative for culture. She was then discharged well with two anti-epileptic drugs. She presented again after 5 months with similar semiology. There was no obvious precipitating factor and Epilim level taken was adequate. CT brain and MRI epilepsy protocol also ruled out structural abnormalities. During her subsequent follow-up, she had developmental regression despite being fit free. Her repeated EEG is consistent with severe encephalopathy with cortical irritability over the left frontal and bilateral occipital.

DISCUSSION

This case highlights that achieving a diagnosis for autoimmune encephalitis and controlling the seizure can be very challenging. Her autoimmune workup was positive for only AMA M2 and lupus anticoagulant, which is not specific for any autoimmune encephalitis. Six variants of the encephalitis receptor autoimmune panel were negative.

CONCLUSION

Autoimmune encephalitis generally responds well to immunomodulators. It is fundamental to control the manifestation of seizure to ensure there is less damage to the cortical structure hence preventing long-term cognitive impairment.

Adult Neurology
PP-A-35

ISOLATED LATERAL GENICULATE NUCLEI HYPERINTENSITIES HERALDING CENTRAL PONTINE MYELINOLYSIS IN OSMOTIC DEMYELINATION SYNDROME; THE "BAGAI TELUR DI HUJUNG TANDUK" SIGN

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INTRODUCTION

Osmotic Demyelination Syndrome (ODS) typically (but not exclusively) results from rapid over-correction of chronic hyponatraemic states. Clinical manifestations vary, and diagnosis depends on interpretation of neuroimaging within relevant historical contexts.
Typical neuroimaging features of ODS include a central-pontine, trident-shaped, T2hyperintense lesion classically indicating central pontine myelinolysis (CPM).[1] Additionally, several extrapontine areas can be affected; collectively demonstrating extrapontine myelinolysis (EPM).[2] Clinicians should be mindful that CPM and EPM can manifest simultaneously, independently, or with temporal discrepancies in their onset.
We present a quintessential case of chronic hyponatraemia over-correction in an eighty-year-old patient who presented lethargic but eventually developed abnormal behaviour, quadriparesis, and spasticity during hospitalisation. Hesitancy in diagnosis and management of ODS were due to abnormally isolated EPM findings on initial MRI.

METHODS

Brain MRI was performed 2 and 4 weeks from presentation.

RESULTS

The initial MRI revealed isolated bilateral lateral geniculate nuclei (LGN) T2/FLAIR-hyperintensities with contrast enhancement but no diffusion restriction. When viewed together with the quadrigeminal cistern, this picture resembles that of two eggs balanced on the horns of a bull: reminiscent of the Malay proverb "Bagai telur di hujung tanduk". While LGN involvement has been implicated in EPM, they have not been reported to occur in isolation from other EPM or CPM changes. The followup MRI later revealed classical trident (and piglet) signs of CPM confirming our suspicion of ODS. LGN lesions had diminished.

CONCLUSION

MRI features of ODS are dynamic and evolve with disease progression. Observed features therefore vary depending on the timing of imaging relative to the natural course of the disease. As demonstrated in this case, the features can initially be limited to EPM without CPM and be extremely isolated to a specific location, such as the LGN. Consequently, clinicians should maintain suspicion for ODS, even in such cases, as early management may improve outcomes.

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Adult Neurology
PP-A-36

A CASE OF IMMUNE-MEDIATED NECROTISING MYOPATHY WITH ANTI-SIGNAL RECOGNITION PARTICLE ANTIBODIES MIMICKING FACIOSCAPULOHUMERAL DYSTROPHY

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INTRODUCTION

Facioscapulohumeral dystrophy (FSHD) is characterised by weakness of the face, shoulder girdle and upper arms. Scapular winging is characteristic of FSHD, and less commonly seen in inflammatory myositis. Here, we report a case of immune-mediated necrotizing myopathy with anti-signal recognition particle (anti-SRP) antibodies who had scapular winging along with facial and proximal upper limb weakness which led to the initial suspicion of FSHD.

METHOD

Case report

RESULTS

A 40 years old man presented with a six-month history of progressive proximal muscle weakness associated with dysphagia. The weakness worsened over the next six months, following which patient required bilateral assistance on walking. There was no significant family history . Examination revealed wasting and weakness of proximal muscles in the upper and lower limbs, nasal speech, and winging of scapula bilaterally. The patient also had wasting of the temporalis muscles associated with mild facial weakness with no evidence of ptosis and extra-ocular muscles involvement. CK level ranged between 2500 to 6600 U/L. Electromyography showed changes consistent with subacute irritative myopathy. Myositis panel was strongly positive for anti-SRP and anti-Ro 52 antibodies. Muscle biopsy of the left quadriceps muscle showed myopathic changes with many atrophic, regenerating and necrotic fibers seen. There was mild to moderate fatty infiltration and endomysial fibrosis. The changes were consistent with immune-mediated necrotizing myopathy. Screening tests for malignancy were unremarkable. Patient completed three days of pulsed intravenous methylprednisolone, followed by tapering dose of prednisolone and maintenance on azathioprine which resulted in improvement of his symptoms.

CONCLUSION

This case illustrates that the clinical presentation of inflammatory myositis can occasionally mimic that of FSHD. Scapular winging, although a typical feature of FSHD, is not pathognomonic of the disease and can occasionally be seen in inflammatory myositis.

Adult Neurology
PP-A-37

MILLER-FISHER SYNDROME MIMICKING MYASTHENIA GRAVIS WITH BULBAR PARALYSIS

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INTRODUCTION

Miller Fisher Syndrome (MFS) is a rare variant of Guillain-Barre syndrome characterized by a triad of clinical features, including ophthalmoplegia, ataxia and areflexia. The initial presentation of MFS could be tricky as the it might mimic other disease such as myasthenia gravis as illustrated in our case. The occurrence of bulbar paralysis in MFS is unusual and when present, should always alarm the clinician. Here, we present a case report of a 41-year-old male patient who presented to our center with an acute onset of diplopia and bilateral eye ptosis with positive ice pack test and was mistakenly treated as myasthenia gravis. The symptom further evolved throughout the admission with new onset of nasal voice, ataxia and areflexia. After comprehensive evaluation, the findings supported the diagnosis of MFS. The patient was initiated on intravenous immunoglobulin (IVIG) therapy, resulting in a gradual improvement of symptoms. The patient's follow-up at four weeks revealed a nearcomplete resolution of symptoms, indicating a favorable outcome.

This case report highlights the clinical presentation, diagnostic workup, and management approach of Miller-Fisher syndrome. Furthermore, we provide a comprehensive review of the current literature, emphasizing the importance of recognizing this distinct variant of GBS. Prompt diagnosis and early initiation of appropriate treatment, such as IVIG therapy, can significantly improve patient outcomes and prevent potential complications.

CONCLUSION

In conclusion, MFS is a rare neurological disorder which can mimic other diseases. Early recognition and diagnosis are crucial for appropriate management and favorable outcomes. Clinicians should be aware of this syndrome and its distinctive features to ensure timely intervention and minimize morbidity associated with this condition.

Adult Neurology
PP-A-38

SUPERFICIAL SIDEROSIS AND DURAL ECTASIA IN A MARFAN SYNDROME PATIENT ON WARFARIN. A CASE REPORT.

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INTRODUCTION

Cerebral **S**uperficial siderosis (cSS) is a rare condition caused by hemosiderin deposition in the subpial layers of the brain and spinal cord due to repeated haemorrhage into the subarachnoid space. Its aetiology includes chronic subarachnoid haemorrhage by trauma, vascular malformations, CNS tumours, cerebral amyloid angiopathy (CAA) or prior intradural surgery or trauma. It has been reported that up to 47-56% of patients with SS have a dural pathology.

METHODS

We describe a 62-year-old Caucasian female with Marfan's syndrome who presented with insidious sensorineural hearing loss and tinnitus for years which deteriorated after an abdominal aneurysm repair. She suffered from type A aortic dissection as one of the complications of Marfan's Syndrome. She subsequently went through Bentall's procedure and mechanical Aortic valve replacement needing lifelong anticoagulation (warfarin).

RESULTS

Patient's Magnetic Resonance Imaging (MRI) of brain showed extensive cerebral superficial siderosis (cSS) and several microbleed. Dural ectasia is a common sequelae of Marfan syndrome and could be the one of the etiologies causing cSS in this patient. Other possible mechanisms which may contribute to cSS in this case include post cardio-thoracic surgery, anticoagulant usage and cerebral amyloid angiopathy.

CONCLUSION

We describe a disseminated cSS and spinal dural ectasia case in a Marfan Syndrome patient. Management decision was complicated by the requirement of lifelong anticoagulation. Dural pathology should be considered in patients with cSS, especially with a background of connective tissue disease, such as Marfan Syndrome.

Adult Neurology
PP-A-39

A SUDDEN PROGRESSIVE SYMMETRICAL LEG WEAKNESS IN A HEALTHY PREGNANT LADY: A CASE REPORT ON ACUTE MOTOR AXONAL NEUROPATHY IN PREGNANCY

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INTRODUCTION

Acute motor axonal neuropathy (AMAN) is one of the uncommon variant forms of Guillain—Barré syndrome (GBS) which has a peculiar feature where it has a special predilection for motor nerves and sparring the sensory nerves. Like GBS, the development of AMAN is also immune-mediated and has been associated with IgG antibodies to the gangliosides GM1, GD1a, GalNac-GD1a, and GD1b, which are present in peripheral nerve axons, causing axonal destruction. It is clinically manifested as progressive symmetrical weakness. It is commonly triggered by antecedent infection, and some cases have been reported to occur after vaccination. However, pregnancy is not a common trigger for AMAN.

METHODS

We report a case of AMAN in an otherwise healthy pregnant lady.

RESULTS

A 31-year-old lady in the second trimester of her sixth pregnancy and has no history of antecedent infection or prior vaccination, presented with progressive ascending bilateral muscle weakness of the lower limbs which ultimately caused her to be unable to walk. Her initial blood investigations revealed no abnormal finding. Her cerebrospinal fluid (CSF) analysis showed cytoalbuminologic dissociation (CSF albumin 329 mg/L, CSF cell count was 0), and her nerve conduction study revealed absent of compound motor action potentials of bilateral common peroneal and tibial nerves, and relatively normal sensory nerve action potentials which suggestive of AMAN variants of GBS. Anti-ganglioside antibody panel was negative. She was successfully treated with immunomodulating therapy and has a good functional recovery. She was discharged with good muscle power recovery and normal deep tendon reflex.

CONCLUSION

This case report illustrates the importance of having high index of suspicion among clinicians to diagnose AMAN in an otherwise normal pregnant lady which can occur in any stage of the pregnancy without any history of antecedent infection or preceding vaccination.

Adult Neurology
PP-A-40

CLINICAL OUTCOMES OF STROKE THROMBOLYSIS IN NON-NEUROLOGIST CENTRE WITH DIFFERENT DOSAGE OF ALTEPLASE: A SINGLE-CENTRE STUDY

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INTRODUCTION

Alteplase is the first line treatment for stroke thrombolysis in Acute Ischaemic Stroke (AIS) as per guidelines with recommended dose of 0.9mg/kg. However, cost is a limiting factor. Although the use of lower dose of alteplase for AIS is yet to be recommended, there is no clear evidence against this practice. Stroke thrombolysis initiated in Hospital Sultan Haji Ahmad Shah (HoSHAS) since 2019 and we aim to illustrate the clinical outcomes of thrombolysis using different dosage of alteplase.

METHODS

This is a cross sectional study of all AIS patients presented to HoSHAS who received alteplase with doses ranging from 0.6mg/kg to 0.9mg/kg due to limited resources from year 2019 until 2023. Their demographic and clinical data were collected and reviewed from the hospital's health information system.

RESULTS

A total of 12 patients who were thrombolysed with alteplase during the period were identified with the mean age of 57-years-old and majority were male (66.7%) and Malay (58.3%). The most common underlying co-morbidity was diabetes mellitus (75%), dyslipidemia and hypertension (25% respectively). 8.3% of the patients had history of stroke, while 16.7% were already on antiplatelet.

The mean time of symptoms onset to thrombolysis was 3.17 hours with the highest National Institute of Health Stroke Scale (NIHSS) of 18/42. 4/12 patients had complication of haemorrhagic transformation and 3 of them were transferred to tertiary centre for further intervention. Unfortunately, 1 patient succumbed. 6/12(50%) of the thrombolysis were successful (improvement of NIHSS score $\geq$ 4) with 2/5(40%) and 4/7(57.1%) of patients received 0.7mg/kg and 0.9mg/kg of alteplase respectively.

CONCLUSION

This study reflects clinical outcome of patients with AIS treated with variable dosage of alteplase and can be an option of treatment where there are limited resources.

Adult Neurology
PP-A-41

A SUCCESSFUL CASE: MECHANICAL THROMBECTOMY (MT)IN ACUTE STROKE WITH LARGE INFARCT CORE

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INTRODUCTION

Multiple clinical trials have demonstrated the safety and effectiveness of mechanical thrombectomy (MT) in large vessel occlusion in a selected patient with restrictive criteria. Several small studies have suggested that patients with large infarct core (LIC) may also benefit from mechanical thrombectomy (MT). Here, we present a case of a LIC successfully treated with MT with an excellent functional outcome.

CASE PRESENTATION

81-year-old gentleman with hypertension and Diabetes Mellitus, presented with left-sided weakness and slurring of speech. The symptoms onset was less than 3 hours with moderate NIHSS score of 15 /42. The diffusion-weighted imaging (DWI) MRI brain shows LIC with core volume of 90mls involving the right MCA territory. The magnetic resonance angiography (MRA) shows right M1 MCA occlusion. We proceeded with MT and managed to achieve complete recanalization of right MCA (TICI 3). Twenty-four hours post MT, the patient's GCS drop, and Computed Tomography (CT) brain shows right intracranial hemorrhage (ICH) with perilesional oedema and mass effect. He was closely monitored as there was no neurosurgical intervention indicated then. Repeated MRI brain on day five postMT shows sustained MCA M1 recanalization, and apparent diffusion coefficient (ADC) shows pseudo-normalization due to reperfusion therapy. He was clinically improved and discharged well with an NIHSS score of 3 and achieved a modified Rankin Score (mRS) of 1 at 3 months post-stroke

DISCUSSION

Large ischemic core of 70–100 mL appears to represent a promising target for MT. A recent meta-analysis has shown that 38.4% and 25.7% of patients with anterior circulation LVO and baseline ASPECTS 0–5 treated with EVT may reach mRS 0–3 and 0–2 at 3months, respectively (1). A total of 12.8% patients developed sICH, while 30% of these died at 3 months (1). When MT was compared with medical therapy, despite a significant increase in the odds sICH, MT was associated with better functional outcomes at 3months. Therefore, MT could be considered in some LIC patients.

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FIGURES

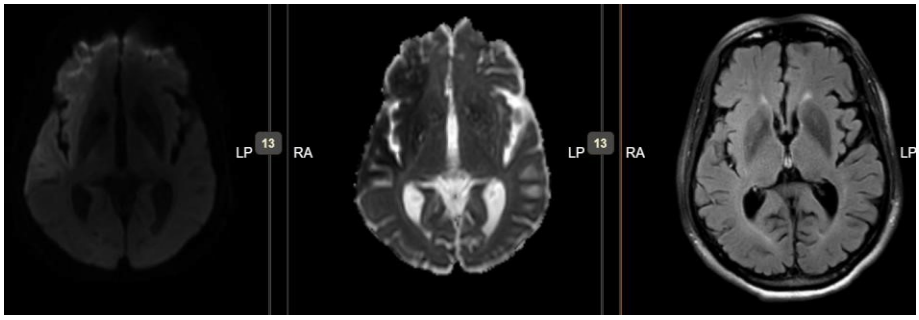

Figure 1: Large DWI core infarct involving right MCA territory. FLAIR signal is preserved in keeping with DWI-FLAIR mismatch

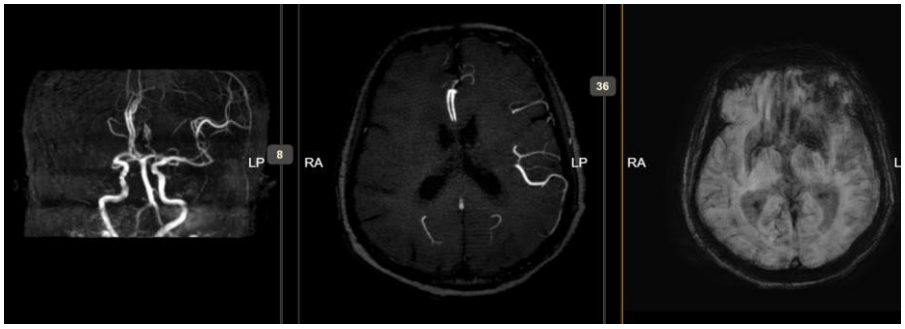

Figure 2: Right M1 segment large vessel occlusion.

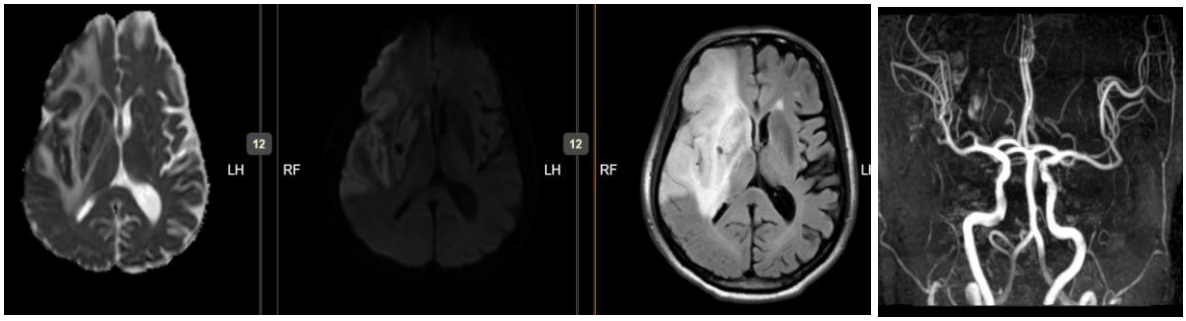

Figure 3: Post infarct shows early ADC pseudo normalization due to reperfusion therapy and M1 recanalization sustained.

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DEFYING ALL ODDS: SUCCESSFUL THROMBOLYSIS IN A NONAGENARIAN WITH POSTERIOR CIRCULATION INFARCT

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INTRODUCTION

Acute Posterior Circulation Infarct (POCI) is often missed owing to its non-specific symptoms. A delay in treatment leads to a poor prognosis and high mortality. There has been an increasing trend of incidence of stroke among the elderly population. However, the treatment of acute stroke in the age group has been challenging due to the lack of data related to the functional outcome and mortality risk. Hence, many opt for conservative treatment.

CASE

This is a case of a previously well 97 year-old female presented to us with worsening left sided weakness upon waking up from sleep, associated with dizziness two days prior. Upon arrival, her Glasgow Coma Scale (GCS) was E3V4M6, BP 162/112mmHg, NIHSS score 10, left sided power 3/5 and right sided power 4/5. Electrocardiogram showed rate controlled atrial fibrillation. Her computed tomography (CT) brain showed P2 segment of right posterior cerebral artery and distal basilar artery thrombosis, with a posterior circulation territory mismatch. She was given intravenous alteplase immediately. Upon discharge one week later, her NIHSS was 5, GCS E4V5M6, mRS 4 (wheelchair assisted) and power bilateral limbs 4/5. She was put on lifelong Apixaban for stroke prevention and subjected for post stroke rehabilitation.

DISCUSSION

The time of occlusion was decided based on the time a patient was last seen well. Elderly patients should not be denied from the standard acute stroke care. Studies have shown that patients aged 80 years and above presenting within 3 hours from symptoms, perform well in intravenous thrombolysis and also thrombectomy. For those presenting with symptoms within 3-4.5 hours, there was no increased risk of intracranial hemorrhage and death.

CONCLUSION

Age should not deter one from receiving standard acute stroke care.

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UNMASKING THE SILENT THREAT : VARICELLA ENCEPHALITIS AS A CAUSE OF CENTRAL NERVOUS SYSTEM INFECTION

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Varicella-zoster virus (VZV) is a DNA virus that belongs to the Alphaherpesvirinae subfamily. After the primary infection, VZV stays in the dorsal root ganglia as a latent infection. VZV can present as various central nervous pathologies such as cerebellar ataxia, arteritis, myelitis, meningitis, and encephalitis. Prevalence of VZV encephalitis occurs in one out of every 33,000– 50,000 cases of VZV. Here we report two cases that shows how prompt recognition and treatment of this infection can decrease its overall mortality.

First case is of a 31 year old female who presented with vesicular rashes and status epilepticus. CT Brain done was unremarkable but CSF analysis yielded a raised protein count of 0.99g/L with normal CSF glucose. CSF rapid polymerase chain reaction (PCR) detected VZV. She was then treated with intravenous acyclovir for a total duration of fourteen days where she managed to make a full recovery.

Our second case is of a 67 year old male who presented with fever and abnormal behavior with prominent rashes following a dermatomal pattern over his left forehead. He then had seizures during the admission. Brain imaging showed old infarcts and CSF analysis biochemistry were normal. CSF rapid PCR that was done revealed VZV. The same regimen of antiviral therapy was administered and he recovered well with rehabilitation and physiotherapy.

In conclusion, the utilization of CSF rapid PCR has played a crucial role in promptly identifying the need for appropriate treatment, leading to not only a remarkable outcome but also allowing targeted therapy thus reducing risk of multidrug resistance which is an ever rising issue.

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A CASE OF A DISABLING, NON-OCCLUSIVE THROMBOTIC STROKE, WHO DIDN'T COME ON TIME

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BACKGROUND

Non occlusive thrombus is rarely described with prevalence ranging from 1.8- 8.1%[1,2,3]. National Institutes of Health Stroke Scale (NIHSS) upon presentation are often non disabling (NIHSS <5) due to continuous antegrade blood flow and outcomes are usually favourable in affected patients[1]. However, for patients who present with high or worsening NIHSS, there are no specific guideline for optimal management.

CASE PRESENTATION

We describe a case of a 46-year-old lady with poorly controlled DM, dyslipidaemia and hypertension who presented to our stroke unit with a wake-up stroke. NIHSS upon arrival was 9. CT brain done at 4.5 hours showed an infarct area of >1.5cm over the left corona radiata, internal capsule and caudate nucleus with an ASPECTS of 8. CTA showed a non-occlusive thrombus (approximately 60% stenosis) at the distal M1 of the middle cerebral artery with good distal opacification. CTP showed a left M1 hypoperfusion of approximately 6seconds on Tmax, CBV was clean and CBF concurring with plain CT. In anticipation of deterioration, patient was put under close observation so arrangements for mechanical thrombectomy (MT) can be escalated if needed. Dual antiplatelet therapy (DAPT) was started and permissive hypertension (SBP kept at 160-180, DBP 70-100) was allowed as hemodynamic compromise may hinder adequate perfusion in the stenosed vessel[1]. NIHSS on day two of stroke was 10 and remained so until discharge at day five of stroke with an mRS of 4. Follow-up at one month showed no improvements.

CONCLUSION

To date, there is no algorithm on management of non-occlusive thrombus. Our patient presented late with an established infarct core hence risk of post thrombolysis hemorrhagic transformation was high while early referral for mechanical thrombectomy was of a debatable benefit, compounded with funding constraints for the latter intervention to be done. Nonetheless, MT was kept as rescue option if patient deteriorated as recent case reports show that it may provide a good outcome[4,5].

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WERNICKE'S ENCEPHALOPATHY AND ITS OUTCOME: A CASE SERIES FROM A TERTIARY CARE CENTRE IN MALAYSIA FROM 2020 TO 2023

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INTRODUCTION

Wernicke's encephalopathy (WE) is an acute clinical condition characterized by confusion, ataxia and ophthalmoplegia. WE is commonly observed in chronic alcohol users or malnourished state like hyperemesis gravidarum. Typical findings in magnetic resonance imaging (MRI) include symmetrical T2 weighted image (T2) hyperintensities in peri-aqueductal gray matter, dorsal medial thalamus and mammillary bodies. WE is a lethal disease. Prompt initiation of treatment can reverse WE. The objective of this study is to describe the clinical, radiological, triggers and outcome of treatment of Wernicke's encephalopathy treated in Hospital Melaka.

METHOD

This case series consists of an observational, cross-sectional and retrospective study (through the analysis of medical records over the past 4 years) of adult patients diagnosed with Wernicke's encephalopathy and the treatment outcomes in Hospital Melaka.

RESULTS

Six patients (1male, 5females) from our center were treated as Wernicke's encephalopathy over the past 4 years, with preceding protracted vomiting. Of these patients, 4 had hyperemesis gravidarum,1 actually had neuromyelitis optica and 1 had persistent vomiting for evaluation. Serum thiamine was only sent for 1 patient due to inavailability of reagents, which showed evidence of thiamine deficiency. 4 of the patients had typical MRI findings. One had MRI findings suggestive of neuromyelitis optica, while one does not have positive MRI findings. All the 6 patients achieved full recovery after 6 months.

CONCLUSION

Wernicke encephalopathy is a reversible medical emergency Hence, we must maintain a high index of suspicion of WE and treat empirically all patients who are at high risk due to the nonspecific and poorly recognized nature of the disease. WE can occur in anyone with nutritional thiamine deficiency, including non-alcoholics. Prompt treatment can prevent permanent neurological morbidity and mortality.

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CADASIL: A CASE REPORT WITH ATYPICAL PRESENTATION

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INTRODUCTION

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy (CADASIL) is a hereditary cerebral arteriopathy caused by mutations in Notch3 gene. It is a small vessel disease which usually presents with ischemic episodes, cognitive deficits, migraine with aura and psychiatric disturbances. We report a case of 27-year-old lady who presented with fever, speech difficulties, headache, blurring of vision, fecal and urinary incontinence. Initial MRI Brain showed multiple symmetrical hyperintense signal intensity on T2 weighted/T2 FLAIR in periventricular and subcortical white matter bilateral frontal and parietal lobes with features suggestive of demyelinating disease, with differential of multiple sclerosis and acute disseminated encephalomyelitis (ADEM). Laboratory findings were unremarkable. She was treated as ADEM and meningoencephalitis. She subsequently developed multiple oral and genital ulcers which was consistent with Behcet's disease on vulva skin biopsy. However, BLA B27 and HLA B51 was unremarkable. She started having syncopal attack, imbalance, lower back pain, forgetfulness, abnormal behavior and psychotic symptoms. Subsequent MRI Brain and Spine showed widespread subcortical and periventricular white matter ischemic changes which may represent CADASIL. She underwent NOTCH3 gene testing which showed a pathogenic p.Arg332Cys mutation.

METHOD

NA

CONCLUSION

CADASIL typically becomes evident in early or middle adulthood with migraine or ischemic event which later manifest itself through recurrent subcortical ischemic strokes leading to stepwise decline and dementia which may result in reduced survival. We need to think of CADASIL in younger patients with small vessel ischemic white matter changes. Radiologically, predilection for anterior temporal lobe white matter is a distinctive feature. Sparing of cortex and subcortical U-fibers is typical. There is no cure or effective treatment for CADASIL at present. Supportive care, including emotional support and counselling is beneficial for patients and their families.

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DIRECT COST OF RITUXIMAB TREATMENT IN MULTIPLE SCLEROSIS: A REAL-WORLD FINDING

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INTRODUCTION

Multiple sclerosis (MS) imposes a significant economic burden on the healthcare system. In 2022, more than half of Neurology budget of Hospital Seberang Jaya was spent on Rituximab, an off-label drug for treating MS. The availability of Rituximab Biosimilar provided an opportunity for self-purchasing or subsidized patients to have a cheaper treatment option. The government contract, however not open for biosimilar drugs. This study aims to estimate the total cost of treatment of MS patients on both Mabthera (originator) and Truxima (biosimilar).

METHODS

A retrospective analysis of MS patients treated with Rituximab from April 2018 to April 2023 was performed. Clinical charts and documented adverse events were reviewed. Healthcare costs were estimated based on Rituximab treatment, hospitalization charge, personnel and other diagnostic costs.

RESULTS

Five patients treated with Mabthera and two patients with Truxima, with follow-up, ranging 1 to 5 years (median: 3 years) were included. Two relapses occurred during follow-up, whereby one Mabthera and Truxima patient, respectively. EDSS score improved in four patients (Mabthera n=3 & Truxima=1), two remained static (Mabthera n=1 & Truxima n=1) and worsened in one (Mabthera=1). MRI imaging reported no new changes in all the patients and a new lesion in one Truxima patient. Urinary tract infection was reported in one Mabthera and Trixuma patient, respectively. The estimated treatment cost of Mabthera was RM 33,920 per patient/year and Truxima RM 16,800 per patient/year. The total estimated personnel cost for a typical 2-day admission without complication is RM 289.50, the diagnostic cost for a complete blood count and urinalysis is RM 11 and the bedding cost is RM 6 for a typical 2 days. The total cost difference in treatment is affected mainly by the Rituximab drug cost unless patients with urinary tract infection on Day 14 are treated and the length of stay prolongs with antibiotics administration.

CONCLUSION

Our findings showed that Mabthera and Trixuma were well tolerated. However, as the number of patients treated with Truxima is limited, a longitudinal cohort or multi-centre approach could be carried out.

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YOUNG ONSET PARKINSON DISEASE

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INTRODUCTION

Parkinson disease is defined by three cardinal symptoms; resting tremor, cogwheel rigidity and bradykinesia. Meanwhile, Parkinsonism is a clinical syndrome that is commonly associated with other etiologies. We report a case of a young onset Parkinson with persistent raised isolated serum copper.

CASE DESCRIPTION

This is a 47 years old lady who was first diagnosed with idiopathic Parkinson at the age of 39. She was first presented with a resting tremor of the right upper limb, associated with stiffness and slow movement. Her initial brain magnetic resonant imaging (MRI) showed no abnormal findings. Further work up for secondary causes of parkinsonism revealed raised serum copper (33.67umol/L) and serum ceruloplasmin (0.75g/L) but absence of Kayser Fleisher ring. Her diagnosis was revised to Wilson's Disease with secondary parkinsonism and she was started on Penicillamine. However, her 24-hour urine copper was normal (0.15umol/24hr) with no evidence to suggest extra copper deposition as her liver function and ultrasound abdomen were normal. Hence, Penicillamine was stopped and she was restarted on Selegiline. However, her motor symptoms continued to fluctuates with peak dose dyskinesia. She was reinvestigated for secondary parkinsonism which revealed persistent raised serum copper (45umol/L) but normal serum ceruloplasmin (0.39g/L) and 24-hour urine copper (0.10umol/24hr). Repeated MRI brain and ultrasound liver also suggest no abnormalities. She subsequently went for deep brain stimulation procedure to control her motor symptoms.

DISCUSSION

In our case, Wilson's disease was ruled out since the repeated serum ceruloplasmin and 24hour urine copper were normal. Isolated elevated serum copper can be caused by acute liver failure of any aetiology, chronic cholestasis or copper intoxication but is not suggestive in this patient.

CONCLUSION

Nevertheless, it is essential to consider alternative diagnosis in a patient with persistent symptoms despite being on optimal medical therapy, especially to rule out secondary causes of Parkinsonism.

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NEUROTUBERCULOSIS: MANY FACES OF A DEVASTATING DISEASE

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INTRODUCTION

Tuberculosis (TB) incidence in Malaysia in 2022 was 25391.[1] Neurotuberculosis has devastating sequalae and high mortality rate. [2] We present 3 previously healthy patients with different manifestations.

METHODS

Case 1

29-year-old woman with meningism for a month. CXR is normal. CT brain shows diffuse cerebral edema and hydrocephalus. Emergency EVD was performed. Intraoperative CSF protein was 1411mg/L and CSF TB GeneXpert detected. MRI shows multiple areas of T2/FLAIR hyperintensity at deep gray matter, corpus callosum, bitemporal, brainstem and cerebellum, which enhances in varying degrees with no restricted diffusion. Leptomeninges enhances diffusely, encasing cranial nerve roots.

Case 2

33-year-old woman with raised intracranial pressure symptoms and fever for a month. CXR shows military TB. Bronchioalveolar lavage TB PCR was detected. CT brain shows multiple lesions with edema causing mass effect, contraindicating lumbar puncture. MRI shows multiple T1/T2/FLAIR isointense nodular ring-enhancing lesions in the cerebrum, cerebellum and brainstem. Some of them show central TI hypointense signal, T2/FLAIR hyperintense signal with restricted diffusion suggestive of central liquid necrosis of tuberculoma. Basal cisterns leptomeninges enhances.

Case 3

26-year-old man with meningoencephalitis for a week. CXR is normal. CT brain shows acute communicating hydrocephalus, necessitating urgent EVD. Intraoperative CSF protein was 1004mg/L and CSF TB GeneXpert positive. MRI shows T2/FLAIR ill-defined hyperintensity at bitemporal and left frontal lobe with no restricted diffusion, with extensive basal meningitis and diffuse pachymeningitis. MRA shows irregularities at left A1/A2 ACA and left M1/M2 MCA suggestive of vasculitis, causing infarction at left internal capsule, corpus callosum and insular region, not seen in previous CT.

DISCUSSION

Neurotuberculosis can present in multiple forms with complications ranging from hydrocephalus, ventriculitis, vasculitis and dural sinus thrombosis. [2]

CONCLUSION

Due to different manifestations of neurotuberculosis, the underlying pathology can be better identified with improved imaging, so early and most appropriate treatment can be provided.

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CASE REPORT :TUMEFACTIVE DEMYELINATING LESIONS IN RELAPSING NEUROMYELITIS OPTICA SPECTRUM DISORDER

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INTRODUCTION

Neuromyelitis optica spectrum disorder (NMOSD) is a severely disabling autoimmune inflammatory demyelinating disease of the central nervous system. Tumefactive demyelinating lesion (TDL) has been rarely reported in NMOSD.

METHODS

A 38-year-old gentleman with no past medical history experienced 5 episodes of recurrent neurological events since 2021. In January 2021, his disease started with intractable hiccups and vomiting .His symptoms resolved spontaneously.
In March 2021, he developed tetraplegia and bowel incontinence . Brain and spine MRI revealed multiple T2W hyperintense lesion at the left frontal white matter region, cervicomedullary junction to C6 level and T2 to T10 level. He received no further workup and treatment. Fortunately, there was a good recovery .
In November 2021, he developed bilateral optic neuritis .Again, in December 2021, he developed left hemiparesis. Both episodes responded favorably to short course steroid.
In February 2022, he developed paroxysmal tonic spasm . Brain MRI revealed multiple white matter lesions at the left frontoparietal lobe, corpus callosum, bilateral periventricular region, and right internal capsule. Spine MRI revealed a T2W hyperintense lesion from the level of the midbrain to C5 . Cerebrospinal fluid shows raised protein of 0.66mg/ml with no cell counts. The oligoclonal band and serum antibody against myelin oligodendrocyte glycoprotein were negative. His serum AQP-4 revealed positive. At last, he diagnosed with NMOSD . IVMP and plasma exchange(PLEX) were started promptly followed by rituximab. His neurological status improved with an expanded disability status scale(EDSS) of 6.0 .
Two weeks after he received rituximab, he developed a focal seizure with dense left hemiplegia.MRI brain showed a new extensive TDL of the right frontoparietal lobe .He received IVMP and PLEX for his relapsed NMOSD.

RESULTS

One month after his discharge, his neurological function showed improvement with EDSS of 8.0. Brain and spine MRI showed treatment respond.

CONCLUSION

NMOSD is a severe condition with disabling outcomes, delayed diagnosis and treatment can lead to subsequent relapses and fatal outcomes.

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CASE REPORT OF PARKINSONISM SECONDARY TO CRYPTOCOCCAL MENINGITIS IN AN IMMUNOCOMPETENT PERSON-AN ELUSIVE CULPRIT

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INTRODUCTION
Parkinsonism among elderly patients remain a common presentation to clinicians.Thorough examination and workout is crucial to finding its etiology and treatment.

METHODS
A 66 years old carpenter presented with persistent giddiness and slowness of movements for 2 years.Family members also noticed that he was unable to recognise close friends and perform daily activities for past one year.He denied any visual hallucinations,clumsiness,or other non motor symptoms of Parkinson's disease.Unfortunately,he developed status epilepticus requiring ventilation and ICU admission.Initial CT(Computed Tomography) Brain showed obstructive hydrocephalus with dilated foramen luschka and magendie.Physical examination post extubation showed hypomimic speech with cogwheel rigidity over left wrist with bradykinesia.There was no cerebellar signs.Initial mini mental state examination(MMSE) showed a score of 20/30.He was empirically started on IV Ceftriaxone 2g BD and IV Acyclovir 500mg TDS.Lumbar puncture was performed showing cerebrospinal fluid of 15g/L with CSF glucose <0.6g/L,however the CSF cell count was zero with culture and sensitivity was no growth.Bedside EEG(Electroencephalogram) showed generalized cortical dysfunction with background 6-7Hz.

RESULTS
MRI brain urgent was subsequently done in view of worsening patient's condition despite of adequate treatment.MRI brain showed ring enhancing non-restricted diffusion DWI cerebellar lesions likely represent tuberculoma and basal cistern thin leptomeningeal enhancement could represent associated tuberculous meningitis.Patient was subsequently started on empirical tuberculous meningitis treatment after a multidisciplinary discussion.Extensive workout including viral screening,Computed Tomography thorax abdomen pelvis for occult malignancy,serum ACE(angiotensin converting enzyme) level was normal.Repeated lumbar puncture revealed CSF containing encapsulated yeast cells on Indian ink stain,Latex crytococcus antigen was positive and CSF culture grew cryptococcus species.Patient was promptly started on IV amphotericin B(0.7mg/kg per day) and oral flucytosine(100mg/kg/day).However,despite of best effort,patient succumbed to infection.

CONCLUSION
A typical parkinsonism with rapid cognitive impairment should warrant an extensive workout.Crytococcal meningitis in an immunocompetent host leading to atypical parkinsonism proves challenging to clinicians.

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MUMMY'S NUMBS AND CRAMPS-A COMMON YET UNSUNG ETIOLOGY

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INTRODUCTION

Numbness and muscle cramps are common symptoms in pregnancy. However, clinician should investigate thoroughly especially if the symptoms are persistent in a pregnant lady.

METHODS

We hereby report a case of a 14 year old nulliparous lady at 7 weeks gestation who presented with subacute onset of bilateral thigh cramping pain, numbness and weakness of 2 weeks duration. Her symptoms were progressive leading to inabilty to stand up and walk. She denied having any upper respiratory tract infection symptoms or gastrointestinal symptoms prior to that. The weakness then gradually involved her bilateral upper limbs especially her hands. However, there was no bulbar, respiratory or facial involvement. There was no restriction of eye movements or clumsiness of limbs as well. Clinical examination revealed areflexic flaccid paraparesis of lower limbs with intact pinprick sensation and proprioception. Upper limb examination showed bilateral wrist drop with preserved proximal arm strength. A clinical diagnosis of acute inflammatory demyelinating polyneuropathy was made.Nerve conduction test done at second week of onset confirmed her diagnosis of GBS with AMAN variant.Lumbar puncture showed normal pressure without cytoalbumino dissociation.She was promptly started on Intravenous Immunoglobulin for 5 days in ward whereby she was managed by a multidisciplinary team.

RESULTS

Workup revealed normal cerebrospinal fluid results except CSF HSV 1+2 Ab IgG was positive. Septic workout done was normal. Anti-ganglioside antibodies sent was negative. Serum electrolytes and Vitamin B12 levels were within normal range. MRI Brain and Spine (noncontrast) was normal. Nerve conduction study showed electrophysiological evidence of AIDPAMAN variant.

CONCLUSION

This case illustrated the importance to consider uncommon cause of paresthesia and cramps which is common among pregnant patients.

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CLINICO-RADIOLOGICAL CHALLENGE: BRAIN LESIONS

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INTRODUCTION

Parenchyma brain lesions have various differential diagnoses. MRI helps in differentiating them.[1] We present 2 challenging patients for discussion.

METHODS

Patient 1

Madam NL, 28-year-old woman with primary mediastinal non-Hodgkin lymphoma achieved remission after standard chemotherapy. PET scan post chemotherapy shows remission. A month later, she presents with raised intracranial pressure and cerebellar signs. Her infective markers are negative.

CECT shows right cerebral and cerebellar enhancing masses with vasogenic oedema and hydrocephalus causing early tonsillar herniation, contraindicating for lumbar puncture.

MRI shows multiple isointense T1 and hypointense T2/FLAIR signals at right frontal, temporal lobe and cerebellum with heterogenous enhancement and restricted diffusion suggestive of hypercellular lymphomatous lesion. This further supported by MRS showing raised choline peak and choline/creatine ratio.

However, her CSF flow cytometry sampled during ventriculoperitoneal shunt insertion is unremarkable.

Patient 2

Madam ZA, 38-year-old woman with acute lymphocytic leukemia achieved remission for 24 years after standard chemotherapy. She presents with a week of right VI nerve palsy and paraplegia.

CT shows no obvious focal brain parenchymal lesion.

MRI shows multiple patchy hypointense T1 and hyperintense T2/FLAIR signals at bifrontal, bitemporal, periventricular, corpus collosum (mainly undersurface), brainstem and cerebellum without enhancement or diffusion restriction, sparing juxtacortical and optic nerve. Spinal cord and cauda equina show long tract myelitis.

CSF protein is elevated (659mg/L) and CSF flow cytometry unremarkable. Serum Anti-myelin oligodendrocyte glycoprotein is positive.

DISCUSSION

Parenchyma brain lesion has many differential diagnoses including lymphoma, tumor, demyelination, abscess and inflammation. The morphology, distribution, patterns of

enhancement and apparent diffusion coefficient mapping of lesion from various MRI sequences help to differentiate diagnoses. [2,3,4,5,6] In situation where procedures are challenging or not feasible, advanced imaging can guide in operative planning.

CONCLUSION

Although advanced imaging aid in diagnostic dilemma, for patient with indeterminate diagnosis, tissue biopsy is diagnostic.

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Adult Neurology
PP-A-54

CEREBRAL VENOUS SINUS THROMBOSIS WITH THROMBOCYTOPENIA, SUCCESSFULLY TREATED: CASE REPORT

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Cerebral venous sinus thrombosis (CVST) is a potentially fatal neurological condition. A 15 years old boy presented to the hospital with right neck swelling, fever, vertigo, and right ear otorrhea with reduced hearing. Neurological examination no abnormalities noted. Contrast-enhanced computed tomography brain showed acute right otitis media with mastoiditis complicated with right transverse sinus, sigmoid sinus, internal jugular vein, and retromandibular vein thrombosis. The precipitating factor for thrombosis is likely due to infection. He was treated with anticoagulant despite having thrombocytopenia. The patient subsequently improved after 6 months of treatment. In summary, patient with concomitant thrombocytopenia can be treated successfully with intravenous heparin inpatient with close monitoring of complications during hospitalization.

Adult Neurology
PP-A-55

A WOBBLY LADY WITH CHRONIC LYMPHOCYTIC INFLAMMATION WITH PONTINE PERIVASCULAR ENHANCEMENT RESPONSIVE TO STEROIDS (CLIPPERS)

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INTRODUCTION

Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) represents a rare central nervous system (CNS) inflammatory disorder which predominantly involves the pons and shows dramatic improvement with steroid.

METHODS

Data from medical records were collected. Clinical features, risk factors, investigations, imaging findings, treatment, and outcomes were recorded.

RESULTS

A 56-year-old lady with underlying hypertension presented with unsteady gait, associated with vertigo and imbalance for 2 month. There was no tinnitus, hearing loss, weakness, numbness, or other cranial nerve symptoms. No raised intracranial pressure symptoms, constitutional symptoms, or any history of stroke or autoimmune disease.

Examination showed severe ataxia with positive cerebellar signs. Systemic examinations were unremarkable. Baseline blood investigations were normal, but she had positive antibody tests for anti-dsDNA 66 IU/ml, Anti RNP/Sm, and Anti PM-Scl 100. Further antibody tests were negative; Anti- Aquaporin 4 receptor, anti-myelin oligodendrocyte glycoprotein (MOG), Autoimmune encephalitis, and paraneoplastic screening.

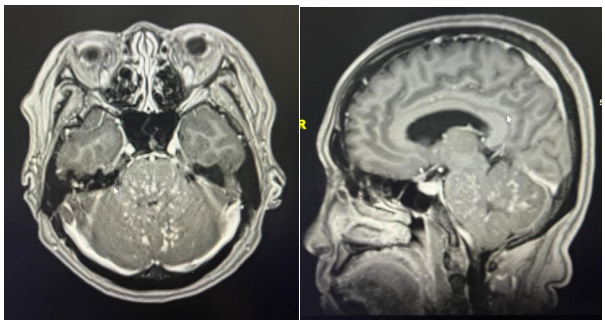
Brain MRI showed abnormalities in the pons, bilateral middle cerebellar peduncle, and bilateral cerebellar hemisphere. The lesion appears hypointense to isointense on T1, hyperintense on T2 and FLAIR, with curvilinear peppering-like or punctate contrast enhancement patterns, and patchy restricted diffusion in DWI and ADC sequence mainly at the enhanced region.MRS shows a choline peak with reduced N-acetyl-aspartate (NAA) at the enhanced area.

She was given intravenous methylprednisolone 1g OD for 5 days, followed by oral prednisolone 1mg/kg body weight. Her ataxia symptom improved dramatically after 5 days of methylprednisolone.

CONCLUSIONS

CLIPPERS is a newly described pontine-centric inflammatory disorder with distinct clinical and radiological features that can also affect the cerebellar area leading to ataxia. The cardinal feature of the condition is a punctate and/or curvilinear gadolinium enhancement, ‘peppering ’ the pons and adjacent hindbrain structures on MRI.

IMAGES



Child Neurology and Developmental Paediatrics
PP-P-01

SEIZURES AMONG CHILDREN ADMITTED WITH COVID-19 IN A MALAYSIAN PAEDIATRIC HOSPITAL

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INTRODUCTION

COVID-19 rapidly spread across the globe starting late 2019, affecting both adults and children. Children tend to have milder disease compared to adults. Seizure is one of the symptoms associated with COVID-19, with studies showing increased seizures during the Omicron wave.

METHODS

A retrospective, cross-sectional, descriptive study was conducted on all children admitted with COVID-19 in Hospital Tunku Azizah (HTA) from June 2021 until May 2022. Demographic and clinical information were obtained from the HTA Paediatric Department COVID-19 database. Further information was obtained from the electronic hospital information system of HTA. Statistical analysis was conducted using chi-square test.

RESULTS

During the study duration, 1586 children were admitted for COVID-19, of which 111 (7%) had seizures. 18 out of 111 (16%) children had previous history of seizure, and 4 (3.6%) were on anti-epileptics. Seizures among children admitted with COVID-19 represented 1.3%-3.4% of COVID-19 admissions from June 2021 to January 2022, increasing from to 9.5% to 18% from February 2022 through April 2022 with a drop to 3.6% in May 2022. Children admitted for COVID-19 between February to May 2022 had higher odds of having seizures compared to those admitted between June 2021 to January 2022 (OR 7.89, 95%CI 2.07 to 13.07, $p<0.001$). A total of 96 (86.5%) children had seizures not exceeding 5 minutes. None of the children required intubation or admission to the paediatric intensive care unit. All children were discharged well.

CONCLUSION

Seizure as a symptom of children admitted for COVID-19 was seen in higher proportions between February 2022 and April 2022, coinciding with the Omicron wave in Malaysia. The seizures were generally not severe and did not require intensive care unit admission.

Child Neurology and Developmental Paediatrics
PP-P-02

THE DIFFICULT FEEDER – FEEDING DIFFICULTIES AMONGST MALAYSIAN CHILDREN WITH AUTISM SPECTRUM DISORDER

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INTRODUCTION

Feeding difficulties is one of the most common challenges in managing children with Autism Spectrum Disorder (ASD). Approximately 25% of children face feeding issues during early years. In children with developmental difficulties, this can be as high as 80%. It is imperative for clinicians to better understand the nature of feeding difficulties experienced before providing appropriate intervention.

METHODS

This is a cross sectional study of children diagnosed with ASD between 1 -7 years on follow up at Child Development & Rehabilitation Centre (CDRC), Hospital Tunku Azizah Kuala Lumpur. The Brief Autism Mealtime Behaviour Inventory (BAMBI) was used to assess children's mealtime behaviours. The BAMBI contains 18 items which is scored by parents in 1-5 point Likert scale. It entails domains of limited food variety (8 items), food refusal (5 items), features of autism (5 items).

RESULTS

Of the 145 children, 65% (93) parents reported feeding difficulties. Predominant problematic behaviours reported by parents were unwillingness to try new food (86.2%) and preference for crunchy textures (64.8%) respectively. The BAMBI mean total score of 39.5 is comparable to similarly studied Asian populations but is significantly lesser when compared to western based populations. This suggest cultural similarities of feeding challenges amongst Asian ASD population. Limited food variety was the primary characteristic reported with a mean of 21.42. Interestingly, 29% of the studied population were underweight (body mass index -BMI < 5^{th} centile). However, no statistically significant association were found between domains of BAMBI and BMI of the children ($r = 0.041$ and $p = 0.622$).

CONCLUSION

BAMBI questionnaire provides an excellent overview to identify feeding difficulties amongst children with ASD. Identifying causative domains of the behaviour enables clinicians to establish focused interventions in managing difficult feeders.

Child Neurology and Developmental Paediatrics
PP-P-03

PERCEPTION OF GENETIC TESTING AMONG PARENTS OF CHILDREN WITH AUTISM SPECTRUM Disorder (ASD)

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INTRODUCTION

ASD is a highly heritable condition and genetic testing is an important consideration in ASD children. The purpose of this study was to explore the perceptions, attitudes, and intentions to pursue genetic testing and their associated factors among parents of ASD children.

METHODS

In this cross-sectional study, 100 parents of ASD children were recruited from the Child Developmental Centre at UKM Specialist Children's Hospital. They completed self-administered questionnaires on perceptions, attitudes, and intentions regarding genetic testing. Descriptive analysis was performed and percentages of parental agreement with questionnaire statements were reported. Association between mean scores for perception and socio-demographic factors were determined.

RESULTS

This study showed that the majority of parents perceived public discrimination (80%) and fewer job opportunities (82%) as the most significant issues faced by ASD children. Only 34% perceived ASD as caused by genes although the majority (83%) of parents believed undergoing ASD genetic testing would contribute to ASD research and help to develop patient-targeting treatment plans (81%). Parents perceived uncomfortable blood-drawing procedure (66%) as a barrier preventing them from undertaking genetic testing in their children and only 54% felt all ASD children should undergo genetic testing. For predictive factors, older parental age was linked to perception of greater ASD severity ($p=0.028$) and more barriers in genetic testing ($p=0.046$).

Presence of family history of ASD increased perception among parents that genes cause ASD ($p=0.030$) and higher perceived benefits of genetic testing ($p=0.003$).

CONCLUSION

Blood-drawing procedures were a barrier for genetic testing. Only about half of parents felt that their ASD children should undergo genetic testing and worryingly, only one-third perceived genes as a cause of ASD. Parents need to be counselled regarding this inaccuracy.

Older parental age increased perception of barriers in genetic testing, whilst having family history of ASD increased perceived benefits of genetic testing.

Child Neurology and Developmental Paediatrics
PP-P-04

ELECTROENCEPHALOGRAM (EEG) AFTER FIRST UNPROVOKED SEIZURE IN INFANTS AND TODDLERS: A RETROSPECTIVE REVIEW

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INTRODUCTION
EEG investigation following first unprovoked seizures in all children is recommended by many guidelines including the Malaysian Paediatric Protocol**.** Our local experience however suggests only a low incidence of EEG abnormality following 1st seizure especially in the toddler age group.

BACKGROUND
To evaluate the detection rate of abnormal electroencephalogram following a first episode of unprovoked seizure in infants and toddlers.

SUBJECTS AND METHODS
Retrospective review of EEG and clinical data from children aged 1 month to 3 years who had outpatient EEG examination in our centre (including those from Klang Valley hospitals) between January 2022 to December 2022.

RESULTS
A total of 906 EEGs were done during the study period of which 390 were in the infant to toddler age group. 56/390 EEG requests were for first unprovoked seizure, and EEGs were performed at mean age of 13.5 months. Three children had further seizures while waiting for the EEG; all three subsequently had abnormal EEGs, suggestive of myoclonic astatic epilepsy in one and focal structural abnormalities in two children. Only 1/53 (1.8%) children with true first seizure had an abnormal EEG, showing focal epileptiform discharges. This girl had a single focal seizure and has not had further seizures 6 months following the EEG.

CONCLUSION
The EEG findings for a first unprovoked seizure in otherwise well toddlers were mostly normal. EEG should be ordered selectively on a case-to-case basis and not routinely, after a first unprovoked seizure in infants and toddlers. Requesting for an EEG following two or more seizures may be more reasonable especially in hospitals without EEG facilities.

Child Neurology and Developmental Paediatrics
PP-P-05

EFFECTIVENESS OF SOCIAL SKILLS GROUP INTERVENTION AMONG CHILDREN WITH MILD AUTISM SPECTRUM DISORDER

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INTRODUCTION

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social communication and functioning, with restricted interests and repetitive behaviours (RRB) beginning in childhood. Many programs have been developed to improve the social skills of children with ASD. One such program is the social skills group (SSG) program, a parent-mediated intervention which has been run by the Child Development Clinic of Sultan Ismail Hospital, Malaysia since 2018. This study aimed to evaluate the effectiveness of the SSG program among children with mild ASD.

METHOD

This was a pre and post intervention study conducted on children with mild ASD who attended the full SSG program held from June to December 2022. The SSG program is a 10-day programme based on the Social Thinking® curriculum. On each day, parents and children attend a 2-hour group session involving an opening routine, story reading and teaching, structured activities to enforce the teaching and a closing routine. The children and parents were assessed using the Social Responsiveness Scale, second edition (SRS-2) and Parenting Sense of Competence (PSOC) 3 times, namely pre-intervention, immediately post-intervention, and five months post-intervention.

RESULTS

During the study period, 22 children with mild ASD between five and eleven years old were recruited. Comparing pre-intervention and immediately post-intervention, there was a significant improvement in median SRS-2 scores (132 to 128, p=0.04) but there was no significant difference during 5 months post intervention. Compared to pre-intervention, significant improvement in median PSOC score (63.5 to 67, p=0.03), communication (45 to 42, p=0.02) and RRB domains (24 to 20, p=0.003) were noted immediately post intervention and the improvement sustained even after 5 months.

CONCLUSION

The SSG program held in 2022 improved PSOC scores, communication and RRB in children with mild ASD and the effect sustained over at least 5 months.

Child Neurology and Developmental Paediatrics
PP-P-06

CHALLENGING BEHAVIOURS IN CHILDREN WITH AUTISM SPECTRUM DISORDER

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INTRODUCTION

Autism spectrum disorder (ASD) is a complex neurodevelopmental disability frequently associated with challenging behaviours (CBs). CBs can be categorized as aggressive or disruptive, stereotypic and self-harming behaviours. Understanding the prevalence and nature of CBs in ASD children could enable appropriate strategies to be implemented, improve on the management of these children and support their families. The objective of this study was to determine the prevalence and types of CBs in children with ASD and its associated predictive factors.

METHODS

In this purposive cross-sectional study, a total of 166 parents of children with ASD aged between 2 to 18 years old from the Child Development Centre in UKMMC between 1st June 2021 till 31st May 2022 were recruited. The Autism Spectrum Disorders – Behaviour Problem for Children (ASD-BPC) questionnaire was translated to Malay and Cronbach's alpha determined to ascertain internal reliability (□=0.9). The recruited parents completed the Malay version of ASD-BPC and demographic questionnaire. The prevalence and subtypes of CBs in ASD children were determined and univariate and multivariate regression was performed to assess predictors for CBs.

RESULTS

The overall prevalence of CBs in ASD children was 89.8%. In terms of CB types, stereotypic behaviours occurred most frequently (75.9%), with repeated and unusual vocalisations found to be the most prevalent behaviour item. Aggressive/disruptive
CBs were reported in 71.7% and self- injurious behaviours were the least commonly described at 16.9%. The predictors for CBs were child age and family income. Lower family income was associated with any CBs (p=0.009) while younger age was associated with stereotypic behaviours (p=0.028).

CONCLUSION

The prevalence of challenging behaviours amongst ASD children attending CDC was high (89.8%), of which the most prevalent type was stereotypic behaviours. Lower family income

was a predictor of challenging behaviours overall, while younger age was a predictor for stereotypic behaviours in ASD children.

Child Neurology and Developmental Paediatrics
PP-P-07

SPECTRUM OF MALAYSIAN CHILDREN WITH SEVERE DYSTONIA: A COHORT STUDY FROM A SINGLE TERTIARY CENTRE.

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INTRODUCTION

Dystonia is the commonest movement disorder in childhood, which occurs due to involuntary co-contraction of agonist and antagonist muscles. We evaluated the clinical characteristics, aetiology, investigations, and pharmacological profile of children with severe dystonia admitted to our centre.

METHODS

This is a retrospective study of children with severe dystonia who were admitted to Hospital Tunku Azizah Kuala Lumpur over two years (1st May 2021 to 31st May 2023). All the relevant data which comprised of the age, clinical characteristics, investigations, medications, and history of hospitalisations due to uncontrolled dystonia were retrieved from the electronic medical records.

RESULTS

A total of 22 children, currently aged between 2-21 years old (median age: 7 years) were admitted due to uncontrolled dystonia. 15/22 (68%) had infantile onset, while 7/22 (32%) had childhood onset dystonia. All were non-ambulant, 18 had global developmental delay/ intellectual disability and eight had co-morbid epilepsy. Aetiology of dystonia was acquired in 10/22 (45%), genetic in 9/22 (41%) and unknown in 3/22 (14%) of children. The children were on a median of three antidystonic medications, with 18 having rescue medications at home, commonest is chloral hydrate (n=13). Gabapentin was the most prescribed medication (n=17), followed by clonidine (n=10), benzhexol (n=10), and baclofen (n=6). Nine children received intramuscular botulinum toxin injection for dystonia control.

The average number of hospitalisations due to dystonia was two (range: 1-5) over the duration of two years with a median hospital stay of nine days (range: 3-42 days). Commonest trigger for hospitalisation was infection. Management during admission included intravenous (IV) hydration, regular chloral hydrate, midazolam infusion, clonidine, and adjustments to the baseline medications.

CONCLUSION

Dystonia is a debilitating condition with significant co-morbidities. Polypharmacy are mostly required for treatment. Despite this, these children are still at risk of developing severe dystonia, most often precipitated by an infection.

Child Neurology and Developmental Paediatrics
PP-P-08

RARE CASE OF A CHILD WITH DUCHENNE MUSCULAR DYSTROPHY AND PALMOPLANTAR KERATODERMA

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INTRODUCTION

Duchenne Muscular Dystrophy (DMD) is an inherited X-linked muscle disease. We present a child with DMD associated with concurrent Nagashima-type palmoplantar keratoderma and amelogenesis imperfecta.

CASE REPORT

Our patient is a 5 year-8 month old boy who presented with lower limb weakness, difficulty in climbing stairs and frequent falls. On examination he was noted to have prominent proximal muscles weakness, absent lower limb reflexes, positive Gower's sign and calf pseudohypertrophy. He was also noted to have bilateral symmetrical thickened skin over bilateral palms since 1 year old which has been worsening with time. Hand examination noted bilateral non transgradient erythema with thick whitish scales sparing central palms and interdigital space. The palms became white spongy in appearance after soaking in water for ten minutes. Plantar region was spared. Examination of his dentition revealed notched upper central incisors. Skin biopsy of palm done showed features of non epidermolytic keratoderma. Genetic studies revealed 3 pathogenic variant identified namely **DMD gene** associated with Duchenne muscular dystrophy, **COL17A1 gene** associated with autosomal dominant amelogenesis imperfecta and epithelial recurrent erosion dystrophy and **SERPINB7** gene associated with autosomal recessive Nagashima-type palmoplantar keratoderma.

CONCLUSION

To our knowledge this is the first case of genetically confirmed DMD associated with concurrent Nagashima-type palmoplantar keratoderma and amelogenesis imperfecta in the Asian population.

Child Neurology and Developmental Paediatrics
PP-P-09

COPING WITH THE STORM: UNVEILING THE EMOTIONAL TURMOIL OF PARENTS OF CHILDREN WITH PEDIATRIC FEBRILE SEIZURES

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INTRODUCTION
Childhood febrile seizures can be a distressing ordeal for parents. This study aimed to evaluate the psychological well-being of parents whose children were hospitalized for febrile seizure treatment. Understanding the impact on parents is crucial, as they bear the primary responsibility for their children's care and welfare.

METHODS
In this cross-sectional study, we enrolled 110 participants whose children were hospitalized for febrile seizures at Hospital Universiti Sains Malaysia between September 2020 and June 2021. To assess their psychological well-being, we utilized a validated Bahasa Melayu questionnaire, namely the Depression Anxiety Stress Scale (DASS-21), to measure levels of depression, anxiety, and stress. Furthermore, we employed multiple logistic regression to identify factors associated with the participants' psychological functioning.

RESULTS
The average age of children experiencing febrile seizures was 21 months, and a majority of these children displayed characteristics consistent with simple febrile seizures (71.8%). Among the participants, the prevalence rates of anxiety, stress, and depression were 58.2%, 29%, and 23.6%, respectively. Upon employing multiple logistic regression and adjusting for other variables, the analysis revealed significant associations between anxiety and child age, family history of febrile seizures, family history of epilepsy, and length of stay in the ward. However, no significant associations were observed between depression and stress when adjusted for other variables. It is noteworthy that participants reported elevated levels of anxiety during their children's hospitalization for febrile seizures.

CONCLUSION
The study identified several factors that influenced parental anxiety, including younger age of the child, absence of a family history of febrile seizures, and longer duration of hospital stay. These findings highlight the importance of conducting further research and implementing interventions aimed at reducing parental anxiety in similar situations.

HEMIPLEGIA AND ENCEPHALOPATHY IN CACNA1A- RELATED DISORDER: A DIAGNOSTIC DILEMMA

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BACKGROUND

Mutations in the CACNA1A gene are associated with episodic ataxia, epilepsy, familial hemiplegic migraine and ischemic strokes. Episodes of hemiplegia can pose significant management difficulties. We describe a girl with CACNA1A mutation with prolonged hemiparesis to highlight the clinical, imaging and electroencephalogram (EEG) features to assist management of future episodes.

CASE HISTORY

An eight-year-old girl with underlying heterozygous pathogenic mutation in the CACNA1A gene presented with acute right hemiparesis (power 0/5), aphasia and encephalopathy associated with vomiting. Prior history revealed two episodes of right sided weakness (one with associated clonic seizure and vomiting) which resolved within 24 hours, and an episode of behavioral arrest following a minor fall. There was never any history of headaches or family history of migraine. Urgent CT brain was normal and MRI (with stroke protocol) only showed cerebellar atrophy. Video EEG monitoring 2 days after admission showed impressive left hemispheric slowing and attenuation and recorded several subtle seizures from the right hemisphere. The seizures and encephalopathy improved following treatment with high dose Topiramate.

DISCUSSION

Differential diagnosis of hemiparesis in CACNA1A mutation include vasospasm related ischaemic stroke, hemiplegic migraine and post ictal paralysis. Urgent imaging should be performed to exclude ischaemic stroke as verapamil is indicated if there is evidence of reversible cerebral vasoconstriction syndrome (RCVS) or aspirin if arteriopathy is seen. EEG is required to exclude electrographic seizures. In our patient, the subtle seizures were only recognized following review of her prolonged EEG monitoring.

CONCLUSION

Hemiplegic episodes in CACNA1A would require urgent evaluation as further management would depend on the identified cause.

Child Neurology and Developmental Paediatrics
PP-P-11

AN INFANT WITH LEIGH/MELAS OVERLAP SYNDROME DUE TO MT-ND6: m.14453G>A MUTATION

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INTRODUCTION

Leigh/MELAS overlap syndrome has been reported in various mitochondrial diseases. It can present with either simultaneous or sequential manner, with Leigh syndrome occurring in an infancy period and MELAS occurring during childhood or elder age. The mutation 14453G>A in the NADH dehydrogenase subunit 6 gene (ND6), though, has been associated with both Leigh syndrome and MELAS, it has not been reported in combination during an acute presentation, especially at an infantile period.

METHOD

Case report

RESULT

A 3-month-old infant who had developmental delay presented with acute encephalopathy and seizure with upper motor neuron findings on examination. He was intubated for respiratory insufficiency. Blood gas showed high anion gap metabolic acidosis. He had persistent hyperlactatemia (range 6-14mmo/L) despite optimal fluid resuscitation. Ophthalmological examination showed retinal microangiopathy, and echocardiography revealed mild ventricular hypertrophy. MRI findings revealed T2 hyperintensities over bilateral basal ganglia and midbrain, with asymmetric abnormal signal intensities over the left temporo-occipital cortex and subcortical regions. Given the aforementioned findings, a genetic testing of the patient's blood-derived DNA identified a de novo heteroplasmic (80%) MT-ND6: m.14453G>A p.(Ala74Val) mutation.

During the hospital admission, he had prolonged ventilation due to central respiratory failure. Hyperlactatemia resolved after oral thiamine and coenzyme Q10 supplementation and seizure was well controlled with levetiracetam. In addition, he needed anti-hypertensive for idiopathic hypertension.

CONCLUSION

Our case report expands the spectrum of mtDNA m.14453G>A, in which it not only illustrated a classical early onset of Leigh syndrome, cardiomyopathy and retinal microangiopathy, it also further elucidated concomitant MELAS findings occurring in a de novo heteroplasmic infant, highlighting the diverse range of clinical spectrum seen in mitochondrial disorders.

Child Neurology and Developmental Paediatrics
PP-P-12

BOYS AND GIRLS WITH ATTENTION-DEFICIT / HYPERACTIVITY DISORDER (ADHD) AT CHILD DEVELOPMENT CLINIC (CDC), HOSPITAL PULAU PINANG (HPP): GENDER DIFFERENCES INPREVALENCE AND CHARACTERISTICS

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INTRODUCTION

ADHD is a common children neurodevelopmental disorder. In Malaysia, the estimated prevalence of ADHD ranges from 1.6% to 4.6% with boys affected 3 to 4 times more likely than girls. We aim to review gender differences in prevalence and characteristics of children with ADHD.

METHODS

A retrospective cohort study was performed involving 91 children with ADHD attending CDC HPP from July 2018 until May 2023. Data pertaining to age and parental concerns at diagnosis, ADHD subtype, sociodemographic factors and response to medications were reviewed.

RESULTS

Our preliminary findings include a predominant male population of children with ADHD, similar to many other CDCs. In a total of 91 children, 74.7% were boys with male to female ratio of 3:1. 63.2% of boys and 56.5% of girls with ADHD have global developmental delay (GDD) or intellectual disability (ID) while 22% of boys and 30.4% of girls with ADHD have Specific Learning Disorder. 25% of boys and 21.7% of girls with ADHD have a concomitant diagnosis of Autism Spectrum Disorder (ASD).

50% of boys and 52.2% of girls first presented to CDC HPP between 4 to 6.11 years, 38.2% of boys and 43.5% of girls at 7 to 12 years old and 11.8% of boys and 4.3% of girls at 2 to 3.11 years.

The highest medical ailment that mothers were afflicted by during pregnancy was gestational diabetes mellitus with 13.2% of boys and 21.7% of girls with ADHD affected.

14.7% of boys with ADHD and 17.4% of girls with ADHD are on medications.

CONCLUSION

We report a male predominance and high comorbidity of GDD or ID and ASD in both girls and boys with ADHD. Majority of children with ADHD first presented between the age of 4 to 6.11 years. Gestational diabetes mellitus was the highest antenatal risk factor.

Child Neurology and Developmental Paediatrics
PP-P-13

PROBLEM BEHAVIOURS AND SLEEP PROBLEMS IN CHILDREN WITH AUTISM SPECTRUM DISORDER: A CROSS SECTIONAL STUDY IN A MALAYSIAN TERTIARY PAEDIATRIC HOSPITAL

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INTRODUCTION

Autism spectrum disorder (ASD) is associated with problem behaviours encompassing emotional and behavioural issues with prevalence of 72-86%. These problem behaviours have negative impact on quality of life and tend to extend into adulthood. In addition, poor sleepers have higher incidence of problem behaviours. Hence, this study aims to determine the percentage of problem behaviours among ASD children and its association with sleep disturbances.

METHODS

This is a cross-sectional pilot study using parent-report Child Behaviour Checklist (CBCL) and Children's Sleep Habit Questionnaire (CSHQ). It composed of 42 children aged 2-12 years diagnosed with ASD who attended Child Development Clinic Hospital Tunku Azizah from 17.05.2023 till 16.06.2023 and excluded parents who did not understand English language and children who were on medication that may affect sleep or behaviour.

RESULTS

16 were from 2-5 years and 26 from 6-12 years. 78.6% comprised of male. Majority were Malay race (75%), followed by Chinese (16.6%) and Indian (7.1%) respectively. 75% of them have sleep problem. Autism spectrum is the most common problem among younger age group (2-5 years) with 68.8% at clinical range and 12.5% at borderline, in keeping with the underlying diagnosis of sample population. When excluding autism spectrum problem, there are 9 (21.9%) children with at least one problem behaviour whereby 7 (16.7%) have concomitant sleep problems. Among younger age group, 24.9% is at clinical range for depressive problem followed by oppositional defiant (18.8%), anxiety (12.5%) and attention deficit/hyperactivity (12.5%) respectively. Similarly, depressive problem (11.5%) is the most common problem encountered in 6-12 years, followed by anxiety (3.8%) and attention deficit/hyperactivity problem (3.8%) respectively. None is at clinical range for oppositional defiant, somatic and conduct problems.

CONCLUSION

Problem behaviours among ASD children is common especially when sleep problem is present with depression being the most. Behavioural assessment should be addressed when managing children with ASD.

Child Neurology and Developmental Paediatrics
PP-P-14

SYMPTOMATIC CARRIER OF HETEROZYGOUS ALPHA-SARCOGLYCAN(*SGCA*) GENE MUTATION: A DIAGNOSTIC DILEMMA

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INTRODUCTION

Limb-girdle muscular dystrophy R3 (LGMDR3 or LGMD2D) is a rare autosomal-recessive muscular dystrophy caused by a mutation in the α-sarcoglycan gene (*SGCA).* Patients often present in childhood with characteristic girdle weakness and calf hypertrophy. Muscle biopsy shows a dystrophic pattern with deficient α-sarcoglycan on immunofluorescence studies. To our knowledge, there has been no report on an autosomal dominant form of *SGCA*-related muscle disorder. Here, we report a child who present with juvenile onset non-specific musculoskeletal symptoms associated with heterozygous *SGCA* mutation.

CLINICAL CASE

A 11 year 8 months old boy, presented with 3 months history of progressive pain and weakness of bilateral shoulders, thighs and legs, accompanied with intermittent chest pain, progressive fatigue affecting daily activities with loss of weight and appetite. Neurological examinations were normal with no myopathic facies, calf muscle hypertrophy and a negative Gower's sign. Other systemic examinations were unremarkable. Laboratory investigations showed persistent raised CK (613-2625 U/L). Cardiac screening was normal. MRI thighs showed patchy areas of non-specific T2 hyperintensity. He was extensively worked up for autoimmune disorders and inborn error of metabolism, which were negative. Muscle biopsy found only mild variations of muscle fibers with few regenerating necrotic fibers and mild endomysial fibrosis, in keeping with a non-specific neuromuscular disorder. Routine immunostaining were normal. Whole exome sequencing (WES) identified only one heterozygous pathogenic variant, missense mutation (C.409G>C), in *SGCA* gene, which confirmed the carrier status of LGMD R3 alpha-sarcoglycanopathy.

CONCLUSION

Our case suggests certain carriers of heterozygous *SGCA* mutation may have mild manifestations by late childhood with non-specific musculoskeletal symptoms and elevated CK. However, we recognise the limitation of WES which might have missed the second pathogenic variant in our patient. More research is needed to delineate the vast variations in the relationship between gene mutations and clinical manifestations of α-sarcoglycanopathy.

Child Neurology and Developmental Paediatrics
PP-P-15

EATING HABITS AND WEIGHT STATUS OF CHILDREN WITH AUTISM SPECTRUM DISORDER AT CHILD DEVELOPMENT CLINIC (CDC), HOSPITAL PULAU PINANG (HPP)

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INTRODUCTION

Children with Autism Spectrum Disorder (ASD) may have selective eating habits and sensory sensitivity that predispose them to poor nutrition. A recent Malaysian study showed prevalence rates of underweight, and obesity were 9.3%, and 21.5%, in ASD children. We aim to review dietary intake and weight status in children with ASD compared with typically developing children.

METHODS

A case-control study involving 60 children with ASD attending CDC HPP from February 2016 until May 2023 and 60 typically developing children from Jalan Perak Health Clinic. Sociodemographic factors and dietary preferences were reviewed from medical reports, parental interview and recorded in data collection form.

RESULTS

Our preliminary findings include a 73.3% predominant male population of children with ASD. 56.5% first presented were between 2 to 6 years old, and 43.5% were 7 to 12 years old.

21.7% of children with ASD were overweight, 58.3% had normal BMI and 20% were underweight.

Parents reported 41.7% of children with ASD as picky eaters, 13% does not like trying new food, 10% likes fast food and 25% were still milk dependent.

25% of children with ASD dislikes vegetables, 13% smelled their food prior to consumption and 3.3% had iron deficiency anaemia requiring supplementation. This study is still in progress, further findings will be presented when completed.

CONCLUSION

In a predominantly male population of children with ASD at CDC HPP, majority had normal BMI but less than half of them had feeding difficulties.

Child Neurology and Developmental Paediatrics
PP-P-16

THE USE OF STEROID THERAPY FOR DUCHENNE MUSCULAR DYSTROPHY IN TERTIARY CENTER- A SINGLE CENTRE STUDY

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INTRODUCTION

Duchenne muscular dystrophy (DMD) is an X-linked recessive dystrophinopathy characterised by progressive muscle weakness and degeneration. The corticosteroid (CS) is the therapy of choice to decelerate the disease progression and to preserve the patients' cardiac and respiratory functions. To date there is a scarcity of literature which reviewed the usage of corticosteroid in children with DMD in Malaysia. Hence, we aim to evaluate the use of corticosteroid among children with DMD in a single tertiary centre.

METHODS

This retrospective cohort study includes all patients diagnosed with DMD before 21 years old from 1 January 2007 to 31 December 2020 with at least 6 months of followup. Data regarding steroid usage, anthropometric measurement, cardiac function and compliance were obtained from electronics health record.

RESULTS

56 patients were analysed; with mean age of diagnosis was 6.1± 2.2 years old. 89.2% (n=50) were started on CS, while the remaining 10.7% (n=6) patients refused steroid therapy. The mean age of initiating CS was 6.39 ± 2.02 years old, with most common regime used is once daily regime (0.7mg/kg/day). 4 of these patients were converted from Prednisolone to Deflazacort due to excessive weight gain, another one due to refusal of Prednisolone. Median age of loss of ambulation in steroid-naïve patients was 9 years old as compared to 10.5 years in those who were taking steroid. 26% (n=15) of these patients has developed cardiomyopathy at the onset of mean age 13.5 years old. 12.5% (n=7) of these patients has restrictive lungs disease, most of them refused non-invasive ventilation. 12% (n=6) of the steroid treated patients has obese.

CONCLUSION

This study showed that most of our cohort were taking steroid therapy and they had a later onset of becoming wheelchair bound as compared to those were steroid -naïve.

Child Neurology and Developmental Paediatrics
PP-P-17

BEHAVIOURAL, ASSOCIATED FACTORS AND DEMOGRAPHIC CHARACTERISTICS OF CHILDREN WITH AUTISM SPECTRUM DISORDER (ASD) IN A TERTIARY-LEVEL UNIVERSITY HOSPITAL IN KLANG VALLEY

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INTRODUCTION
Autism Spectrum Disorder (ASD) is a neurodevelopmental condition in childhood presenting with impairments in socialization and communication as well as unusual behaviours. Children with ASD were compared with typically developing (TD) children to assess factors associated with ASD and presence of early behavioural issues in a tertiary-level hospital in Klang Valley.

METHODS
In this cross-sectional study, children aged 18 months to 18 years were recruited from the Universiti Kebangsaan Malaysia Medical Centre, including children diagnosed with ASD from Child Development Centre and typically-developed (TD) children attending nursery and general paediatric clinics, between 1st January to 31st December 2018. TD children underwent screening for neurodevelopment issues and ASD using MCHAT and ESAT. Demographic data and a questionnaire of behavioural and other factors were obtained.

RESULTS
A total of 301 ASD and 68 TD children matched for sex and age were recruited (n=369). Comparing ASD and TD children, ASD children were more likely to be firstborn (p= 0.004, OR 2.44 95% CI: 1.33 to 4.50), had increased risk of comorbidities (p= <0.001, OR 3.56 95% CI: 1.94 to 6.52), and were more likely to have a family history of developmental delay (p< 0.001, OR 7.12 95% CI: 3.31 to 15.34). ASD children were more likely to have abnormal behaviours (p= 0.003, OR 6.09 95% CI: 1.83 to 20.30) and greater likelihood of tantrums (p< 0.001, OR 4.64 95% CI: 2.11 to 10.21) in infancy compared to TD children.

CONCLUSION
ASD children were found to have differences when compared to TD children, with a greater likelihood of being firstborn, having comorbidities, and a family history of developmental delay. Parents of ASD children were more likely to report abnormal behaviours including tantrums even in early infancy.

INFANTILE SPASMS IN EXTREME IMMATURITY: THE UNIVERSITY OF MALAYA MEDICAL CENTRE EXPERIENCE

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INTRODUCTION

The improvement in survival of extremely immature infants following advancements in neonatal critical care will result in a growing cohort of infants with intracranial injuries of immaturity and a propensity to infantile spasms (IS). We sought to describe the clinical characteristics of extremely immature infants treated in our centre who developed IS following discharge from the neonatal intensive care unit (NICU).

METHODS

A retrospective chart review of extremely immature infants (born before 28 completed weeks of gestation) treated in the University of Malaya Medical Centre was performed. Patients born between 1 January 2019 and 31 December 2023 were included. Exclusion criteria were non-citizen status and death before discharge.

RESULTS

Three patients were diagnosed with IS (median age of onset 10 months; range 7.5-11 months). Median gestational age was 26 weeks, 2 days (range 23 weeks-26 weeks, 6 days) and median birth weight was 795 g (range 580-960 g). The incidence of IS in all infants born at extreme immaturity was 3.2% (3/93). Diagnosis of IS was confirmed with electroencephalography (EEG). Severe intraventricular haemorrhage (IVH) (grade III-IV) with periventricular leukomalacia was present in all three patients – an incidence of IS of 12.5% (3/24) among extremely immature infants with severe IVH. All patients had bronchopulmonary dysplasia, with a median duration of oxygendependence of 51 days (range 38-154 days).

CONCLUSION

Further research into the characteristics of extremely immature infants who develop IS will provide an impetus to improve neurocritical care in the NICU to reduce the risk of development of this catastrophic epileptic encephalopathy among extremely immature infants.

Child Neurology and Developmental Paediatrics
PD_P_02

DEVELOPMENTAL PROFILE AND CHARACTERISTICS OF CHOCHLEAR IMPLANT CANDIDATES – A SARAWAK EXPERIENCE

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BACKGROUND
In 2020, Sarawak General Hospital Child Development Clinic adopted standardised developmental tool as a part of cochlear candidacy evaluation. The initiative aimed to ensure that children referred with profound sensorineural hearing loss are assessed comprehensively with Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III).

METHODS
Consecutive referrals by Otorhinolaryngology Department between June 2020 and October 2022 were included in the single-centre cross sectional descriptive study.

RESULTS
There were 12 referrals received with mean age of 17 months at presentation and ethnicity comprises of 41.6% Malay as well as Indigenous, while the remaining 16.8% were Chinese. Parental first concerns were unresponsive to noise (33.3%), speech delay (58.3%) and failed hearing screening test at birth (8.4%). Additionally, 33.3% had poor social interaction with onset of first concern. Of the cohort, 25% had significant events during intrapartum period (ie abruptio placenta, foetal bradycardia) however had good APGAR scores. Other perinatal risk factors include gestational diabetes mellitus (25%), prematurity (25%), low birth weight (67%) and congenital Cytomegalovirus infection (8.4%). Mean composite score for Cognitive domain was 76; 33% fell within the Average range, 42% were in the Below Average range and 25% were well below average. Mean composite score for Motor domain was 74 with equal distribution into the Average, Below Average and Well Below Average range. With regards to comorbidity, a third of candidates have Autism Spectrum Disorder and 17% have malformation (Goldenhar Syndrome and Dandy Walker Malformation). 25% were not selected for implantation. Out of 9 selected candidates, 8 received cochlear implant and 1 acquired auditory brainstem implant.

CONCLUSION
Majority of cochlear implant candidates referred for developmental assessment have Cognitive and Motor domain scores above the -2 standard deviation. There is a higher incidence of Autism Spectrum Disorder in this cohort.

Child Neurology and Developmental Paediatrics
PD_P_03

AGO1 MUTATION IN ANEUPLOIDY: A CASE OF NEURODEVELOPMENT DISORDER WITH EPILEPSY

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INTRODUCTION

Argonaute 1 (AGO1) mutation has been reported leading to syndromic form neurodevelopment disorders and seizures in recent years. We present a case of AGO1 mutation who has a concomitant Klinefelter Syndrome (KS). Early developmental delay, intellectual disability and frequent seizures which are incongruous with phenotype of KS suggested possibilities of other concomitant gene mutation in this case.

METHODS

The propositus developed first afebrile seizure at 3-years-old, with seizures recurring at the age of 5. The semiology was focal in nature with impaired awareness. His epilepsy was difficult to control initially, requiring two anti-seizure medications. Subtle dysmorphism, including small and upturned nose, narrow palpebral fissure, and prominent incisors were observed. Additionally, he had significant delays in cognitive, motor, speech and language domain, consistent with a later diagnosis of intellectual disability, requiring special education. He remains seizure free since 11-year-old and no longer requires any anti-seizure medication currently.

RESULTS

Karyotype revealed 47, XXY.
Fragile X Analysis was negative.
Whole exome sequencing revealed heterozygous pathogenic variant of c.595G>A (Gly199Ser) in AGO1 gene.
Initial serial EEGs showed no epileptic discharges before findings suggesting self-limiting focal epilepsy of childhood were revealed on the latest EEG.
MRI Brain detected no abnormality.

CONCLUSION

When signs and symptoms are incongruent with the primary diagnosis, exome sequencing is a useful tool to be considered for possible dual or multiple genetic diagnosis. This has important implications for improving accuracy of genetic counseling, determining the correct prognosis and consequently, organizing the best long-term follow-up.

Child Neurology and Developmental Paediatrics
PD_P_04

FATAL CONGENITAL MYOTONIC DYSTROPHY: A DIAGNOSIS NOT TO BE MISSED!

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Congenital myotonic dystrophy is the most severe form of myotonic dystrophy, characterised by respiratory insufficiency, severe hypotonia and generalised muscle weakness at birth.

We present a late premature baby who required active resuscitation and invasive ventilation at birth due to respiratory failure. He had hypotonia, hyporeflexia, myopathic facies with high arched palate and minimal spontaneous movements & breathing effort. Unfortunately, he became ventilator dependent and did not show significant improvement over time. Inherited metabolic screening, TORCHES, chromosomal study and SMN gene testing were negative. Initial questioning did not reveal any family history of muscle weakness in parents or immediate family members. However, baby's mother was noted to have proximal muscle weakness when met a few weeks post delivery and she attributed this to an alleged motor vehicle accident. Further examination of mother revealed classical signs of myotonic dystrophy and electromyography showed characteristic myotonia pattern with divebomber sound .Whole exome sequencing showed a heterozygous pathogenic variant c.*224CTG (62) at DMPK gene.

Congenital myotonic dystrophy is a rare but crucial differential diagnosis to be considered in neonates who present with severe hypotonia and respiratory failure. Early establishment of diagnosis is vital for genetic counselling and to help in management as well as prognosis.

Child Neurology and Developmental Paediatrics
PD_P_05

THE NEUROLOGICAL SPECTRUM OF PRESENTATION AND SEQUELAE IN CHILDREN DUE TO JAPANESE ENCEPHALITIS (JE) IN PERAK, MALAYSIA.

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OBJECTIVE

Japanese encephalitis is the most common endemic encephalitis worldwide with no definitive treatment to date. We describe the neurological presentation and sequelae of 3 children with JE encephalitis.

METHODS

A retrospective case review was performed. Informed consent was obtained from the parents of patients.

CASE REPORT

We describe 3 cases of JE who presented to our centre with fever and constitutional symptoms such as vomiting, cough, and reduced oral intake. All 3 had a deterioration in conscious state at day 3-4 of illness and deteriorating neurological status by the first week of illness. Case 1, a six-year-old, presented progressive encephalopathy, aphasia, prominent tremors and asymmetric UMN signs. Case 2, a fouryear-old presented with encephalopathy, aphasia and left hemiparesis. Case 3 presented with hallucination and behavioural abnormalities that progressed to encephalopathy, generalised hypertonia, and subsequent refractory dystonia. All three children had MRI changes in thalami with or without basal ganglia and substantia nigra involvement. All children had serological confirmation of JE IgM in CSF or serum. All were given intravenous immunoglobulin at the third to 4th week of illness. The child with isolated involvement of thalami (case 1) had the most rapid recovery with no motor deficits four months post-illness, case 2 developed near complete recovery after 6 months and case 3 continued to have severe neurological impairment at 1-year post-acute illness.

CONCLUSION

Japanese Encephalitis is an important cause of acquired severe neurological disability in endemic regions in Malaysia. Regional vaccination programs should be expanded to include the regions with increasing cases.

Child Neurology and Developmental Paediatrics
PD_P_06

CASE REPORT OF A CHILD WITH SEVERE PRESENTATION OF NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD) – AQUAPORIN-4 ANTIBODY POSITIVE

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INTRODUCTION
NMOSD is a severe autoimmune central nervous system disease that rarely occurs in childhood. We describe a 10-year-old girl with severe presentation of NMOSD.

METHODS
We conducted a retrospective review of case notes.

CASE REPORT
Our patient was a 10-year-old girl with underlying bronchial asthma who presented with a 3-week history of gastrointestinal (GI) symptoms (epigastric pain, frequent hiccups, and constipation). In the 3rd to 4th week, she complained of headaches, blurring of vision, difficulty in swallowing and ambulation/movement with subsequent progression to difficulty in breathing. She required ventilatory support for 3 weeks. Examination revealed severe bulbar weakness (absent cough and gag reflexes) and limb weakness (hypotonia, absent reflexes and power 1-2/5 bilateral upper and lower limbs with no sensory involvement) as well as autonomic dysfunction (hypertensive urgency, tachycardia, bowel dysmotility and bladder dysfunction). Her Expanded Disability Status Scale(EDSS) was 9.5. Ophthalmological examination revealed blurred optic discs bilaterally in keeping with optic neuritis. MRI revealed high signal intensities on T2 weighted and Flair sequences at the posterior inferior surface of the medulla oblongata and caudal end of the 4th ventricle, keeping with area postrema syndrome. Blood and CSF samples both revealed AQP4 antibody positivity. She showed no response to intravenous immunoglobulin and minimal response to highdose intravenous steroids. After 5 cycles of therapeutic plasma exchange, she showed improving neurological recovery, EDSS 7.0.

CONCLUSION
NMOSD should be suspected in children/adolescents with persistent unexplained GI symptoms with progressive neurological dysfunction.

Child Neurology and Developmental Paediatrics
PD_P_07

ABSTRACT CONGENITAL MYOPATHY 19 CAUSED BY A NOVEL HOMOZYGOUS MUTATION OF THE PAX7 GENE

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INTRODUCTION

PAX7 plays a role in the development of cephalic neural crest derivatives and in maintaining the population of satellite cells in postnatal muscles. Mutations of PAX7 are associated with congenital myopathy 19 (CMYP19) and are characterized by infantile onset of progressive muscle weakness, muscle atrophy, impaired walking, scoliosis, and dysmorphic facial features. To date, there were 4 families reported to have CMYP19.

METHODS

We report a 4-year-old boy with a novel mutation in the PAX7 gene causing CMYP19.

RESULTS

The child is a product of a non-consanguineous marriage between two individuals living in neighbouring villages. He had an uncomplicated prenatal and perinatal history. Postnatal examination revealed left undescended testis. The first symptoms noticed in the neonatal period were poor sucking and difficulty breastfeeding. He has dysmorphic facial features which include bilateral ptosis, down-slanting palpebral fissures, micrognathia, high-arched palate, hypotonic facies and thoracic kyphosis. Neurological examination revealed axial hypotonia, generalized muscle weakness, waddling gait, generalized atrophy of skeletal muscle and preserved deep tendon reflexes. The child has global developmental delay with preserved cognition. Results for cardiac screening, creatinine kinase, thyroid function, PTPN11, SMN and tests for Prader Willi were normal. Whole Exome Sequencing (WES) revealed a homozygous mutation at PAX7: c.742G>T; p.Glu248Ter, confirming the diagnosis of CMYP19.

CONCLUSION

Our findings describe the clinical features of a child with CMYP19 caused by a novel variant of PAX7, which expands the current understanding of the clinical and molecular spectrum of this rare disease. Our case is also unique as it is the only 1 out of the 5 affected families without a history of consanguinity. Furthermore, this case elucidates the growing importance of WES in resolving diagnostic dilemmas faced in our day-to-day practice.

Child Neurology and Developmental Paediatrics
PD_P_08

NEUROREGRESSION WITH MYOCLONUS IN A PAEDIATRIC PATIENT WITH POST-SARS-COV-2 INFECTION

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INTRODUCTION

The recent pandemic SARS-CoV-2 has caused significant medical co-morbidity and mortality. Current data with regards to myoclonus related to SARS-CoV-2, especially in children, is limited. Our case illustrates post-SARS-CoV-2 infection manifestation can very rarely simulate subacute sclerosing panencephalitis, with seemingly lingering neuroinflammation despite glucocorticoid treatment.

METHODS

Case report

RESULTS

We present a boy whose SARS-CoV-2 test was confirmed positive in both nasopharyngeal secretion and cerebrospinal fluid. He developed myoclonus soon after respiratory symptoms. EEG revealed periodic high voltage polyphasic discharges over the central region and at times time-locked with myoclonic movements, resembling Rademecker complexes. MRI brain was normal. The myoclonus was refractory to various antiseizure medications and intravenous immunoglobulin. His cognition and neurological function continued deteriorating in the subsequent months – slurred speech, unsteady gait and frequent falls due to refractory myoclonus. Although his myoclonus was later completely controlled with glucocorticoids, he was spastic quadriparesis, with modified RAN scale 5. A repeat lumbar puncture revealed an elevated neopterin, despite six months of glucocorticoid treatment. A repeat MRI showed diffuse abnormal signal intensities over both grey and white matter. Although pulsed rituximab was given to him in light of the ongoing neuroinflammation, the neurological function remained poor, without any improvement in modified Rankin scale.

CONCLUSION

Post SARS-CoV-2 infection can lead to an immune-mediated panencephalitis. The evidence of immunotherapy in this entity is still inadequate due to limited studies.

Child Neurology and Developmental Paediatrics
PD_P_09

A CASE SERIES – AUTISM SPECTRUM DISORDER & SCURVY: RETURN OF THE GREAT MASQUERADER

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INTRODUCTION

Prevalence of Autism Spectrum Disorder (ASD) has been on the rise globally for decades. Feeding disorder among children with ASD is a well-recognized comorbidity that should receive equal if not more attention than the core communication deficits & repetitive behavior that define autism. Nonetheless, many clinicians remained oblivious to the importance of managing feeding difficulties which could lead to potentially reversible nutritional disorders, such as scurvy, a disease caused by prolonged severe dietary deficiency of ascorbic acid. Scurvy can present with a wide array of clinical manifestations that could mimic malignancy, orthopaedic, rheumatological, haematological and neurological illnesses. Diagnosis of scurvy in children with ASD requires high index of suspicion in view of their language impairment. They are also particularly at risk of nutritional deficiencies considering their highly selective and restrictive diet preference.

METHODS

This study presents two case reports of ASD patients presented to Sarawak General Hospital with signs and symptoms suggestive of scurvy.

RESULTS

In this case series, we illustrated two patients with laboratory confirmed scurvy among children with ASD, who presented with painful knee swelling, and persistent limping respectively. They received treatment dose of ascorbic acid supplementation following diagnosis and achieved symptom resolution without complications.

CONCLUSION

Review of children with ASD mandates meticulous exploration of diet history to actively identify children who are at risk of scurvy so that timely intervention can be reinstituted as complication of scurvy could be detrimental.

Child Neurology and Developmental Paediatrics
PD_P_10

CO INFECTION OR CROSS REACTIVITY? THE DENGUE ENCEPHALITIS AND JAPANESE ENCEPHALITIS CONNUNDRUM.

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INTRODUCTION

Dengue and Japanese encephalitis are vector borne zoonotic diseases caused by Dengue virus and Japanese encephalitis (JE) virus respectively. These infections cause significant morbidity and mortality especially in South East Asian region where both are endemic. As both of these viruses belong to the Group B Flavivirus and share the same vector, it is not uncommon for them to present with similar clinical features and cross reactive serological results.

METHODS & RESULTS

We report a 11 year old boy who initially presented with fever and status epilepticus but he remained encephalopathic despite optimal medical treatment. The CSF analysis showed lymphocytosis (90%) with raised protein and MRI brain at day 5 of illness showed encephalitic changes involving deep gray matter and brainstem. He was initially treated as para infectious encephalitis with immunotherapy but showed minimal neurological recovery and developed extrapyramidal symptoms. The serum JE and Dengue serology (IgM) were later positive. However, given the constellation of clinical presentation, CSF analysis and MRI brain findings, we concluded the diagnosis of Japanese encephalitis.

CONCLUSION

As both Dengue and Japanese encephalitis are endemic in Malaysia, it is not uncommon for co-infection or cross reactivity to occur. Therefore, a thorough clinical and laboratory assessment correlating with neuroimaging is crucial to make an accurate diagnosis.

EFFICACY AND TOLERABILITY OF TRANSDERMAL SCOPOLAMINE PATCH FOR THE MANAGEMENT OF SIALORRHEA IN CHILDREN WITH DISABILITY

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INTRODUCTION

Sialorrhea or drooling is defined as an overflow of saliva from the mouth, usually associated with oral motor dysfunction, insufficient swallowing ability, a deficit of the oral sphincter or, less frequently, with an increase in saliva flow. Sialorrhoea is a common problem in children with disability, especially in children with cerebral palsy with around 40% prevalence in a population-based study. Recent studies have emerged showing the effectiveness of transdermal scopolamine patch (TSP) in controlling sialorrhoea in paediatric patients. Objectives: This study aimed to determine the efficacy and tolerability of TSP for the management of sialorrhea in children with disability.

METHODS

The studied subjects were all children with disability, presenting with severe sialorrhoea who was started with transdermal scopolamine patch (TSP), in Paediatric rehabilitation unit, Cheras Rehabilitation Hospital, Malaysia. The severity and frequency of sialorrhoea was scored using parental reported symptoms, via Drooling Severity and Frequency Scale (DSFS) : mild (1-3), moderate (4-6), severe (7-9). The significant efficacy was defined as reduction in the category of severity.

RESULTS

A total of 8 patients (5 male) was identified. The mean age of commencement of TSP was 9.8 years (range : 6-16). Six of them (75%) were diagnosed / suspected to have genetic disorders while 2 had cerebral palsy. Global developmental delay was noted in all of these children. The duration of treatment was 1 to 2 years in 4 of them and more than 2 years in 3 (1 defaulted follow up). The TSP showed significant efficacy in 6 out of 7 of patients (85.7%) during the last follow up. TSP was generally well-tolerated with only 3 complained of localized allergic reaction.

CONCLUSION

This study shows that TSP is efficacious in controlling the sialorrhea in children with disability. It is also well-tolerated with minimal side effects. Future large study and meta-analysis will be good to confirm this finding.

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EPILEPSY AND NEURODEVELOPMENTAL COMORBIDITIES OBSERVED IN A PAEDIATRIC TUBEROUS SCLEROSIS COMPLEX CLINIC

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INTRODUCTION

Tuberous Sclerosis Complex (TSC) is a neurocutaneous genetic disorder that involves many organ systems, including brain, eyes, heart, kidney, and skin. This condition is associated with neurodevelopmental comorbidities.

METHOD

The paediatric neurology team in Hospital Tunku Azizah Kuala Lumpur runs a TSC clinic every month. On referral, the patients would be reviewed by the paediatric neurology team following the clinic protocol. Patients would receive 6 monthly clinic reviews, annual renal ultrasounds and 3 yearly brain magnetic resonance imaging surveillance.

RESULTS

Between August 2022 and July 2023, a total of 60 patients aged 1 to 21 years old (median age of 10) attended the TSC clinic. Thirty-two (53%) patients were male. Five (8.3%) patients never had seizures. Forty-six (83.6%) of the 55 patients with seizures had onset before 2 years old, of which 26 presented with infantile spasms. All 55 patients received anti-seizure medication while 10 patients underwent brain surgery. During the latest clinic review, 35 (63.6%) patients were still on anti-seizure medications, with 20 patients receiving 2 or more anti-seizure medications. 31 patients (56.4%) were still symptomatic, having daily (n=4), weekly(n=5), monthly (n=10) and yearly (n=12) seizures. The children had neurodevelopmental comorbidities including Autism Spectrum Disorder (n=18), Attention Deficit Hyperactive Disorder (n=5), Intellectual Disability (n=3) and learning difficulties but not specified (n=11). The 53 children who were above 4 years old were attending mainstream schools (12, 22.6%), special needs education (27, 50.9%), community based program (3, 5.7%) or not in any program or work (11, 20.8%).

CONCLUSION

TSC is a multisystem disorder that commonly presents with seizures and developmental problems, requiring anti-seizure medications and developmental support. A well-structured review plan would guide a holistic approach to the patient.

Child Neurology and Developmental Paediatrics
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SCN1A MUTATION IN HEMICONVULSION -HEMIPLEGIA-EPILEPSY (HHE) SYNDROME.

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INTRODUCTION

Hemiconvulsion-hemiplegia-epilepsy (HHE) syndrome involves initial sudden and prolonged unilateral convulsive seizures, followed by transient or permanent hemiplegia and epilepsy during early childhood. Neuroimaging characteristically shows brain atrophy more pronounced on the hemisphere
contralateral to the side of hemiplegia with dilatation of the ventricular system. The role for *SCN1A* genetic mutations in the development of hemiconvulsion–hemiplegia–epilepsy (HHE) syndrome has not been clearly described. Many variants, including those in CACNA1A, ATP1A, HNRNPU AND SCN1A,have been noted in patients with HHE but a common, pathogenic variant is yet to be identified.

CASE REPORT

We describe a 2 year old boy with history of febrile seizure who presente/d with status epilepticus requiring ventilation. He subsequently developed superrefractory focal status epilepticus with left sided hemiplegia. MRI brain shows abnormal signal intensity at right frontoparietal and temporal region, mainly involving the cortex with diffuse edema, right head of caudate nucleus and bilateral thalamus. There is also hyperintense signal on T2W, FLAIR and shows restricted diffusion on ADC/DWI, consistent with HHE. Immunotherapy both methylprednisolone (30mg/kg/day) and intravenous immunoglubulin (2g/kg) was initiated. We subsequently screened for *SCN1A*, that showed a heterozygous variant *c.2123delC* that is likely pathogenic and has genetic potential associated with HHE.

CONCLUSION

Early recognition and seizure control is important to prevent the development of hemiplegia and intractable epilepsy in HHE. We suggests that *SCN1A* genetic mutation is a rare predisposing cause of HHE syndrome, that further needs to be reported.

Child Neurology and Developmental Paediatrics
PD_P_14

CASE REPORT: RARE INFANTILE ONSET OF MELAS WITH *MT-TS1* GENE MUTATION

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INTRODUCTION

Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS) is a multisystem disorder. This condition is relentlessly progressive, resulting in neurological impairment and cognitive decline. We present an infant with early onset MELAS here.

METHODS

A previously well 4-month-old infant presented with recurrent episodes of cyanosis associated with apnoea that was confirmed by video-EEG to be unprovoked focal seizures with impaired consciousness. She was small for age, hypotonic with global developmental delay. Initial EEG showed frequent bursts of focal epileptiform discharges lateralized to right temporal region. Subsequent EEGs evolved into bilateral and multifocal independent epileptiform discharges, followed by electro-decremental activities. MRI Brain showed bilateral symmetrical restricted diffusion at caudate and lentiform nuclei. In the subsequent month, at 5-months of age, she developed intermittent episodes of feeding intolerance with vomiting. Additionally, she was diagnosed to have infantile onset diabetes mellitus when she developed persistent hyperglycaemia that was a challenge to manage. Her developmental milestones regressed and she remained encephalopathic. Mitochondrial encephalomyopathy was suspected and she started on vitamin cocktail and Co-enzyme Q. Unfortunately, there was no improvement and she developed refractory epilepsia partialis continua as well as diabetic ketoacidosis at 8 months old and succumbed.

RESULTS

Whole Exome Sequencing revealed homoplasmic likely pathogenic variant m.7512T>C in *MT-TS1*.

CONCLUSION

This case could be the youngest patient reported so far suffering from MELAS due to mitochondrial gene *MT-TS1* gene mutation. Mitochondrial cytopathy should be considered as a differential diagnosis for early onset diabetes mellitus, particularly with concurrent neurological manifestations / multiorgan involvement. Homoplasmic mutation in this patient contributes to atypical early presentation, along with more severe and rapid disease progression.

Child Neurology and Developmental Paediatrics
PD_P_15

ALERD AND ITS 'BRIGHT TREE' : A CASE REPORT

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INTRODUCTION

Acute encephalopathy refers to insult to the brain that presents with seizures and impaired consciousness. Acute leukoencephalopathy with restricted diffusion (ALERD) is a clinical-radiological syndrome and is one of the infection associated encephalopathy seen in children. ALERD can be classified into diffuse and central-sparing ALERD. Diagnosis is based on identifying the restricted diffusion in the white matter of cortex on DWI, commonly described as the bright tree appearance (BTA).

CASE REPORT

We describe a 3 year old boy with previous history of febrile seizure who presented with prolong status epilepticus requiring ventilation and cerebral protection. He empirically received ceftriaxone and acyclovir with the initial suspicion of meningoencephalitis. Post extubation he was persistently encephalopathic and later developed generalized seizures requiring increase in anit-seizure medication. We initiated intrvenous immunoglobulin 2g/kg suspecting autoimmune encephalitis. However later MRI revealed diffusion restriction and T2 prolongation of cortical and subcortical regions, especially bifrontal and biparietal hemisphers with relative central white matter sparing suggestive of diffuse ALERD.He was commenced on methylprednisolone 30mg/kg/day. He showed some motor recovery including improve head support and moves all limb against gravity. However he appeared dyskinetic with poor oromotor recovery. We initiated monthly pulses of intravenous methylprednisolone observing for recovery.

CONCLUSION

ALERD is a rare cause of acute encephalopathy that typically has a biphasic clinical course with a bright tree appearance on MRI. Early treatment with pulse steriods and anti seizure is the treatment of choice. Tocilizumab use in central sparing ALERD with high interleukin-6 (IL-6) has been reported, with the hypothesis that IL-6 plays a pivotal role in the pathogenesis of ALERD. This needs further evidence and reports.

Child Neurology and Developmental Paediatrics
PD_P_16

SJOGREN-LARSSON SYNDROME (SLS): A CASE REPORT ON A RARE INBORN ERROR OF LIPID METABOLISM CAUSING GLOBAL DEVELOPMENTAL DELAY.

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INTRODUCTION

Sjogren-Larsson syndrome (SLS) is an autosomal recessively inherited disorder of lipid metabolism due to the lack of activity of microsomal fatty aldehyde dehydrogenase (FALDH) characterized by ichthyosis, spasticity and intellectual disability.

CASE REPORT

Our patient is a 2 year old girl who first presented to us at 3 months of age with faltering head growth and scaly skin. She is of South Indian ethnicity and is a product of a consanguineous union born prematurely at 36 weeks 5 days with no antenatal or intrapartum complications. She showed initial progress in her development with subsequent tapering and regression after the age of one. Between the ages of one to two years she was noted to have significant motor delay with generalised spastivity with lower limb predominance and became aphasic with loss of learnt speech. Her skin findings were in keeping with generalised icthyosis and eye assessment revealed crystal like deposits around the fovea. A Magnetic Resonance Imaging (MRI) done at this point revealed volume loss with an elevated lipid peak on spectroscopy in keeping with SLS. This was genetically confirmed via whole exome sequencing that revealed a pathogenic homozygous mutation is the ALDH3A2(+) which is associates with SLS.

CONCLUSION

SJS is rare genetic disorder that should be suspected in children with delayed development, spasticity, and ichthyosis.

Child Neurology and Developmental Paediatrics
PD_P_17

TUMEFACTIVE ACUTE DISSEMINATED ENCEPHALOMYELITIS A DIAGNOSTIC ENIGMA OF CYSTIC LESIONS.

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INTRODUCTION

Tumefactive demyelinating lesions are an uncommon manifestation of demyelinating disease that mimic primary central nervous system neoplasms and can pose a diagnostic challenge. Although a biopsy may be required to distinguish tumefactive acute demyelination encephalomyelitis (ADEM) from neoplasms or infection, certain ancillary and radiographic findings may preclude the need for invasive diagnostic procedures. These pseudotumoral lesions are commonly associated with myelin oligodendrocyte glycoprotein (MOG) antibody associated demyelination, ADEM and neuromyelitis optica spectrum (NMO).

CASE REPORT

We report a 4 year old boy who presented with bilateral lower limb weakness, altered behaviour and pica. He was treated in our district with the initial suspicion of ADEM, initiating methylprednisolone 30mg/kg/day for 5 days. He developed polyfocal neurological deficits with persistent irritability, despite 5 days of steroids. MRI on day 6 of steroids showed multiple cystic white matter lesion at the bilateral frontal lobes largest measuring 3.1 x 1.4 x 2.6cm with mass effect on bilateral lateral ventricles. We added on intravenous immunoglobulin 2g/kg in view of poor recovery with steroids. Parents were counselled for biopsy but unfortunately not agreeable. 2 weeks after immunotherapy, he showed tremendous motor recovery as he walked without support and fed himself with some assistance. Speech was still impaired with poor articulation.

CONCLUSION

Tumefactive demyelination is a rare phenomenon in patients with ADEM. Diagnosis can be made on clinical and on radiological grounds. Biopsy is typically definitive and confirmatory, revealing perivenular inflammatory cell infiltration and demyelination in ADEM. Patients with tumefactive ADEM typically exhibit an excellent response to corticosteroids, and the disease is typically monophasic.

Child Neurology and Developmental Paediatrics
PD_P_18

ISOLATED OPHTHALMOPLEGIA IN CEREBRAL VENOUS SINUS THROMBOSIS IN PAEDIATRIC. A CASE REPORT

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INTRODUCTION

Cerebral sinus venous thrombosis (CSVT) is a rare and serious yet treatable cause of acute neurologic syndromes in paediatrics. CVST often misdiagnosed due to non-specific clinical manifestation which can be subtle in paediatric age group. Morbidity and mortality are significant but management remains controversial. The lack of evidence supporting treatment and anxieties about safety of anticoagulation lead to dilemma for the optimal treatment of the disease.

CASE REPORT

Here is a 5-year-old boy, with a history of mastoiditis and otitis media 2 weeks earlier, presented with sudden onset esotropia of left eye without any other symptoms including headaches or diplopia. Clinically he had restricted lateral gaze of left eye (LE) corresponding to 6th cranial nerve palsy. The rest of the cranial nerves were intact. Fundoscopy revealed bilateral papilloedema. No other signs of increase intracranial pressure or neurological deficits were seen. Cranial CT scan revealed right transverse sinus thrombosis. He was started on fluid rehydration and intravenous Ceftriaxone. CSVT were affirmed later by CT Venogram showing involvement of right transverse sinus, right sigmoid and right internal jugular vein (IJV). Ultrasound doppler of the neck, however, showed good patency of both IJV. It was finally decided to start him on anticoagulant therapy (fondaparinux) as his esotropia failed to improve with conservative treatment, though he remained very well. After 4 weeks, his LE esotropia had fully recovered with no adverse effect of treatment. Papilledema was still present. MR venography showed partial resolution of CSVT with residual thrombosis seen in right transverse and sigmoid sinuses without any brain parenchymal changes.

CONCLUSION

CSVT may have subtle presentation including new onset ophthalmoplegia in a well child. This may pose a therapeutic dilemma. Children who failed conservative therapy or have extensive venous involvement should be treated with anticoagulation. Fondaparinux can be a safe and effective option.

Child Neurology and Developmental Paediatrics
PD_P_19

A RARE ALERD CASE FOR ACUTE ENCEPHALOPATHY IN CHILDREN (ACUTE LEUKOENCEPHALOPATHY WITH RESTRICTED DIFFUSION)

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INTRODUCTION

Acute leukoencephalopathy with restricted diffusion is a distinct clinico-radiological entity which characterized by acute encephalopathy with characteristic MRI findings, involving predominantly white matter. It is believed to be immune-mediated process as it is often triggered by infection. Though varied neurological outcomes were reported this far, there were almost two-third of them associated with significant neurological sequelae or even mortality.

METHOD

Case study

RESULTS

A 2 year-old girl who had underlying autistic spectrum disorder presented to a district hospital for pneumonia. She was discharged on day 3. However, within the day of discharge, she developed febrile status epilepticus for two hours. Seizure was aborted with loading intravenous (IV) phenytoin. She was intubated and admitted to PICU for ventilation support. She had hypertonia and hyperreflexia in all four limbs with ankle clonus. Lumbar puncture was done after 3 days of cerebral protection. Although clinical findings and CT brain were initially suspected of meningoencephalitis, CSF result was not suggestive of that. An urgent MRI brain revealed symmetrical abnormal signal intensity with restricted diffusion involving bilateral rostrum and genu of corpus callosum, subcortical white matter in bifrontal regions, caudate nuclei and basal ganglia. Meanwhile, she started developing choreoathetoid limb movements while sedation was weaning down. IV Immunoglobulin was initially administered for her, but the dyskinetic movements did not improve. Furthermore, she was irritable and remained encephalopathy after extubation. Intravenous methylprednisolone was instituted and the abnormal movements became less and resolved after five days of IV methylprednisolone. She regained her baseline neurodevelopmental function with no dyskinetic movements upon discharged.

CONCLUSION

MRI brain is imperative in investigating any children who present with acute encephalopathy, especially in establishing the ALERD diagnosis in our patient. We believe that cerebral protection and timely immunotherapy could have improved the neurological outcome if the diagnosis is made early.

Basic Neuro Science
OP_B_01

NEUROPROTECTIVE ROLE OF LITHIUM-MEDIATED REST RESTORATION IN DOWN SYNDROME INDUCED PLURIPOTENT STEM CELL (IPSC)-DERIVED NEURONS

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INTRODUCTION

Down syndrome (DS) is the most common genetic cause of intellectual disability and early onset of ageing. Individuals with DS typically have impaired neurological development with neuropsychiatric disorders. Repressor Element-1 Silencing Transcription factor (REST) which is the key initiator of epigenetic neuronal geneexpression modification, has been reported to be dysregulated in DS human and mouse models. Encouragingly, previous studies have proven the ability of lithium to induce REST activation in ageing neurons. Hence, this study aims to investigate the neuroprotective potential of lithium to restore REST expression in DS induced pluripotent stem cell (iPSC)-derived neurons, thereby improving the neuropathologies seen in DS.

METHODS

Three pairs of isogenic wildtype and DS iPSC cell lines were procured. The iPSCs were differentiated into neural stem cells (NSCs), and then into neurons. Subsequently, immunocytochemistry (ICC) was performed at each developmental stage to characterize the properties of cells. The neurons were then treated with 10mM of lithium for 24 hours. After the lithium treatment, ICC and Western blot (WB) were performed to measure the expression of REST, and also synaptic markers PSD95 (postsynaptic) and Synaptophysin (pre-synaptic), to assess possible improvements in neural functions.

RESULTS

ICC results revealed positive staining of Oct4 for all iPSC lines, positive staining of Nestin for all differentiated NSCs, and positive staining of Tuj1 for all differentiated neurons, indicating a successful differentiation process from iPSCs to neurons. WB and ICC results revealed that REST expression was restored in the lithium-treated DS neurons compared to the non-treated DS neurons. The expression of synaptic markers was also upregulated in the lithium-treated DS neurons.

CONCLUSION

In conclusion, it is encouraging that the dysregulation of REST expression in DS can be rescued by lithium. Hence, repurposing lithium could be an impactful contribution towards the discovery of therapeutic strategies in DS neuropathologies.

Basic Neuro Science
OP_B_02

ELUCIDATION ON THE FUNCTIONAL ROLE OF MICRORNA-21 AS AN ANTI-INFLAMMATORY KEY SWITCH IN α7nAChR ACTIVATION IN PREVENTING CEREBRAL ISCHAEMIC REPERFUSION INJURY

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INTRODUCTION

Ischemic stroke is characterized by a sudden loss of blood flow in an artery leading to the brain. The activation of the α7-Nicotinic Acetylcholine Receptor (α7nAchR), which is found in immune cells such as microglia, has shown promising results in improving inflammatory profiles in stroke-induced rats. Here, we investigated the role of microRNA-21 in mediating inflammation via α7nAchR activation in preventing cerebral ischemia-reperfusion injury.

METHODS

The mouse BV2 microglia cell line was kept in hypoxia chamber to mimic ischemic injury and preconditioned with PNU 120596 (a 7nAchR agonist) to activate the receptor. Later the protein and gene expression of M1 and M2 markers as well as other downstream signalling pathways (NF-kB and STAT) was measured by qPCR and ELISA. Antagomir of MicroRNA-21 was transfected to investigate the protective role of microRNA-21.

RESULTS

The optimum time point of OGD was finalized after measuring cell viability at different time points (1,2,4,6,8 hours) using MTT assay. 4 hours was established as the optimum time point as it showed more than 80% cell viabilty as well as successful inflammation. The activation of α7nAChR by an agonist inhibited the OGD/R-induced elevation of pro-inflammatory markers (TNF-a, IL-6, and IL-1B) while increasing the expression of the anti-inflammatory factor IL-10. It was also discovered that after OGD/R, NFkB p65 levels increased significantly, whereas α7nAChR activation significantly reduced its expression. Interestingly, the inhibition of microRNA-21 reversed the anti-inflammatory effects of α7nAChR.

CONCLUSION

The results demonstrate that activation of α7nAChRs inhibits the transformation of M1 microglia and promotes the M2 phenotype regulated by NFkB and STAT3 pathways and microRNA-21 provide a key role in this process.

Basic Neuro Science
OP_B_03

SUBACUTE METHIOPROPAMINE IMPAIRED COGNITIVE FUNCTION AND INCREASED MOTOR ACTIVITY IN MICE

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INTRODUCTION

Methiopropamine (MPA), a derivative of methamphetamine (METH), is one of the new psychoactive substances (NPS) which are a range of drugs designed to mimic the effects of illicit drugs. NPS have become increasingly popular due to easy access to their supply sources but limited research on their long-term health consequences has raised concerns about their potential neurotoxicity. This study investigated the subacute effects of MPA on cognitive function, anxiety-related and depressive-like behaviour using a battery of tests in mice.

METHODS

Male Swiss Albino mice were randomly divided into four groups (n=10) which received daily intraperitoneal injections of either normal saline, METH at 1 mg/kg or MPA at 1 or 3 mg/kg once daily for seven days. The animals were subjected to novel object recognition (NOR), open-field (OFT), 8-radial arm maze (8-RAM) and forced swim (FST) tests at the end of the treatment.

RESULTS

Mice treated with MPA and METH demonstrated intact non-spatial memory on day 7 but MPA at 3 mg/kg significantly ($p<0.05$) caused memory deficits 24 hours postwithdrawal using NOR test. Similarly, the higher dose of MPA impaired reference and working memory errors comparable to METH based on the 8-RAM test. MPA did not induce depressive-like behaviour as evident by unaltered immobility time in the FST. In the OFT, MPA at 3 mg/kg reduced anxiogenic behaviour accompanied by increased locomotor activity.

CONCLUSION

Subacute MPA treatment induced cognitive impairment upon withdrawal and demonstrated increased motor activity in mice. This study contributed to the understanding of behavioural consequences of their use which poses a threat for public health requiring the development of policies to regulate NPS.

Basic Neuro Science
OP_B_04

NOVEL *PARK7*/*DJ-1* FRAMESHIFT MUTATION IN A MALAY FAMILY LEADS TO LOSS OF EXPRESSION AND IMPAIRED MITOCHONDRIAL FUNCTION IN PATIENT-DERIVED FIBROBLASTS

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INTRODUCTION

About 5–10% of Parkinson's disease (PD) cases are early onset (EOPD), with *GBA1*, *PRKN*, *PINK1* and *SNCA* genes being most frequently implicated, while mutations in the autosomal recessive *PARK7/DJ-1* gene are rare and less investigated. We report the discovery of a novel *PARK7/DJ-1* mutation in two Malay siblings with EOPD, and the observed pathogenic effect on mitochondrial function.

METHODS

DNA from the two siblings was first screened using the CENTOGENE PD gene panel. Segregation analysis of the identified candidate variant in *PARK7/DJ-1* was performed amongst the affected siblings and one unaffected sibling, and further variant screening was conducted in 300 ethnically-matched, neurologically normal controls, using Sanger sequencing. *DJ-1* RNA and protein expression was measured from cultured skin fibroblasts from the affected siblings and 3 controls. Mitochondrial membrane potential and oxygen consumption was measured using Seahorse and TMRE to assess the effect of the mutation on mitochondrial function.

RESULTS

Both patients had early onset disease at 34- and 37 year-old respectively, complicated with severe motoric and cognitive impairment. A novel homozygous single nucleotide deletion (c.245delT) resulting in a frameshift (p.Leu82fs) in *PARK7/DJ*-1 was identified in both patients. This variant was absent in an unaffected sibling and in 300 Malay controls. RNA and Western blot analysis revealed a significant loss of DJ-1 expression in the patients. An abnormal exon 4 skipping event, producing a non-functional *DJ-1*$^{\Delta ex4}$ transcript was also observed. Functional assays indicated that there was lower mitochondrial membrane potential and impaired oxygen consumption rates in patients' fibroblasts.

CONCLUSIONS
We postulate that the homozygous *DJ-1* single nucleotide deletion is causal for EOPD in this Malay family, and the pathogenic effect is mediated through impaired mitochondrial function, leading to neuronal loss. Importantly, this study adds to the limited literature on the mutational spectrum in *DJ*-1, especially among under-represented populations.

KEY WORDS
DJ-1, PARK7, mitochondria, Malay

Basic Neuro Science
OP_B_05

SMALL FIBER NEUROPATHY ANIMAL MODEL DEVELOPMENT USING LOW DOSE STREPTOZOTOCIN AND HIGH FAT DIET-INDUCED TYPE 2 DIABETIC IN RATS

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INTRODUCTION

Small fiber neuropathy (SFN) is one of the microvascular complications in Type II Diabetes Mellitus (TIIDM) patients where lack of diagnostic tools and late in diagnosing the disease is the major contribution to a more severe neuropathy in the patients. Early detection and intervention on SFN may halt the disease progression and according to USFDA, development of new drug should begin with animal model of disease. To date, no established SFN animal model was developed to serve as a platform to understand the pathogenesis of SFN as well as a screening tool for new drug developments. Thus, our aim is to develop SFN animal model by using low dose Streptozotocin (STZ) and high fat diet (HFD)-induced TIIDM in rats.

METHODS

TIIDM was induced in *Sprague Dawley* (SD) rats using low dose of STZ (35 mg/kg, i.p.) after 2 weeks on HFD. Rat's body weight and random blood glucose level were monitored every two weeks, started when the HFD was introduced (week 0). Von Frey filament study and intraepidermal nerve fibers (IENF) density were also performed on week 0, 4 and 8 to observed the development of small fiber neuropathy in rat's animal model.

RESULTS

Low dose of STZ and HFD caused a significant increase in the random blood glucose level in the diabetic group (30.9±1.96) as compared to the normal control group (7.4±0.78). Rat's body weight was increased over time in the normal control group (419.9±25.10), while diabetic group (323.3±12.86) showed a reduction in the body weight once the diabetic was established. Diabetic group showed a significant reduction in both IENF density (6.9±0.43) and nociceptive threshold (22.3±6.40) as compared to normal control group (11.1±0.84 and 60.0±0.11) respectively.

CONCLUSION

Low dose STZ with combination of HFD protocol is recommended for the establishment of small fiber neuropathy in SD rat animal model.

Keyword: Small fiber neuropathy (SFN), Intraepidermal nerve fiber (IENF) density, Von Frey filament study, Sprague Dawley (SD) rat, Type II diabetes mellitus (TIIDM)

Basic Neuro Science
OP_B_06

COMPARING REWARD FUNCTIONAL CONNECTIVITY IN LATE ADOLESCENTS USING N-BACK TASK: AN FMRI STUDY

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INTRODUCTION

Reward is known to motivate anyone into work and decision-making. Different brain activations were discovered when participants chose to receive monetary rewards for themselves or their parents. Reward research in Malaysia is more focused on self-monetary rewards. This study aims to measure the difference in reward functional connectivity (FC) between those who choose either a monetary reward for themselves (cash group) or their parents (filial group).

METHODS

Fourteen healthy Malaysian participants (mean age 23.24 ± 0.70) were measured with 3 Tesla MRI. FC was analysed via Conn Toolbox. Participants were shown a block design with four runs (2 blocks per run). Each block has a cue picture shown followed by the n-back task. Four cues were shown: the picture of money, parents, a certificate, and a round neutral object.

RESULTS

Participants were divided into cash (n=7) and filial (n=7) groups, determined by their highest n-back score. The left and right nucleus accumbens (lNAcc; rNAcc) were set as the seed, due to their major role in the brain's reward system. For cash>filial groups, significant increases in FC are observed from lNAcc to the left superior temporal gyrus and left precentral gyrus during the cash cue, and are thought to be attributable to decisions of self-monetary reward. A significant increase in FC from rNAcc to the right cerebellum during the filial cue might be associated with an altruistic context. For filial>cash groups, significant increases in FC are observed from lNAcc to the left inferior lateral occipital cortex and left parietal operculum cortex during filial cue, suggesting an association with reward and attention. There is no significant difference in FC between rNAcc and every voxel in the brain during the cash cue.

CONSLUSION

Overall, our findings indicate that cash and filial cues are associated with different patterns of FC in both groups.

Basic Neuro Science
OP_B_07

EFFECTS OF KRATOM (MITRAGYNINE) ON CHRONIC UNPREDICTABLE MILD STRESS-INDUCED DEPRESSION IN SPRAGUE-DAWLEY RATS

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INTRODUCTION

Depression is a mood disorder that can lead to a loss of cognitive function. Mitragynine, a major alkaloid of kratom plant has been reported to exhibit antidepressant effect. Hence, the aims of this study are to determine the potential antidepressant effect of mitragynine in chronic unpredictable mild stress (CUMS)-induced depression, a model used to imitate depression in human. This study further aims to investigate the effect of mitragynine on the CUMS-induced cognitive deficit.

METHODS

Male Sprague-Dawley rats (250g) were subjected to CUMS procedure for six weeks and body weight was measured every week. After 4 weeks of CUMS, animals were treated with fluoxetine, mitragynine or lyophilized kratom decoction (LKD) for 2 weeks. Then, a battery of behavioral testing such as open field test (OFT), forced swim test (FST), elevated plus maze test (EPM), social interaction (SI) and Morris water maze (MWM) tasks were performed.

RESULTS

The results showed that mitragynine treatment significantly improved the distance travelled and the number of rearing in OFT and the climbing time in FST. In EPM task, fluoxetine and mitragynine increased the number of entries and time spent in open arm. Furthermore, fluoxetine and mitragynine treatment mitigated the reduction in the time spent in target quadrant by CUMS in MWM while in SI task, fluoxetine, mitragynine and LKD enhanced the social interaction time.

CONCLUSION

Taken together, this finding suggests that mitragynine was able to alleviate the CUMS-induced depression and cognitive deficit. This finding further indicates the therapeutic potential of mitragynine as an antidepressant.

Basic Neuro Science
OP_B_08

DELIVERY OF EMBELIN-POLOXAMER 188 NANOMICELLES ACROSS CELLULAR MODEL OF THE BLOOD-BRAIN BARRIER

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INTRODUCTION

Therapies for neurodegenerative disorders like Alzheimer's disease face challenges due to the blood-brain barrier (BBB), which limits drug delivery to the brain. Nanomicelles have emerged as a promising strategy to overcome this barrier. This study aims to investigate the enhanced ability of embelin-Poloxamer 188 nanomicelles to penetrate the BBB using a porcine brain endothelial cell (PBECs) model, assessed through the transendothelial electrical resistance (TEER) assay. Embelin, a natural compound derived from *Embelia ribes Burm.f.*, exhibits potent antineurodegenerative properties but suffers from limited aqueous solubility, hindering its bioavailability. Previous research has demonstrated that combining embelin with an amphiphilic carrier improves its bioavailability. Poloxamer 188 (P188), a non-toxic triblock copolymer, has shown neuroprotective effects and the ability to restore cell membrane integrity in Alzheimer's disease. Combining embelin and Poloxamer 188 is expected to have a synergistic effect, enhancing BBB permeability and facilitating improved delivery of embelin to the brain.

METHODS

To assess the cytotoxicity of the nanomicelles on PBECs, MTT assay was conducted prior to the establishment of the BBB model, where the capillary fragments, isolated from the brain cortices of a 5-6-month-old domestic pigs were cultured with puromycin-containing medium until the pBECs reached up to 95% confluency before being transferred onto permeable membrane filter inserts.

RESULTS

Cytotoxicity studies using the MTT assay demonstrated no apparent toxicity on PBEC barrier function when treated with embelin-Poloxamer 188 nanomicelles for 1 hour, even at concentrations up to 100 µg/ml. Permeability studies showed an increased apparent permeability coefficient (P_{app}) in the apical to basolateral (blood-to-brain) direction across the PBEC monolayer compared to unmodified free embelin.

CONCLUSION

These findings suggest that embelin-Poloxamer 188 nanomicelles have the potential to enhance drug delivery across the BBB, providing a promising avenue for the treatment of neurodegenerative disorders.

Basic Neuro Science
OP_B_09

CEREBROSPINAL FLUID LACTATE LEVEL AS A SIGNIFICANT DISCRIMINATOR FOR CSF BACTERIAL INFECTION IN NEUROSURGICAL PATIENTS

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INTRODUCTION

Early identification of cerebrospinal fluid (CSF) bacterial infection in neurosurgical patients is pertinent. However, common markers such as CSF cell counts, glucose and protein level are often affected by the presence of blood, concurrent usage of steroids while formal culture is time-consuming. Thus, we retrospectively compared and explored the potential of using CSF-lactate as an indicator for bacterial infection.

METHODS

We retrospectively retrieved data of all neurosurgical patients who had undergone CSF sampling procedures in PPUKM from 1 Jan 2022 until 30 May 2023. All CSF samples that were sent for CSF-lactate level were included. Samples without biochemistry and culture & sensitivity result, or without concurrent bedside blood glucometer reading as well as repeated sample from the same patient within 48 hours was excluded. CSF-lactate level was compared between samples with and without culture confirmed bacterial infection and analyzed using independent student t-test. Other parameters including CSF-protein, CSF-glucose, blood white cell count (WCC) and C-reactive protein (CRP) level were compared similarly as well.

RESULTS

A total of 78 CSF samples from 37 neurosurgical patients in PPUKM were included.
CSF-lactate level in these samples ranged 1.0mmol/L to 11.8mmol/L (mean 3.351 +/- 1.592). From all samples, there are two samples with culture confirmed bacterial infection (2.6%). Mean CSF-lactate level is significantly higher in samples with bacterial infection compared to those without (7.6mmol/L vs 3.2mmol/L, $p<0.001$). In another hand, CSF-glucose, CSF-protein, blood WCC and CRP level were not significantly different between these two groups of samples. However, CSF:blood glucose ratio was also differed in between these groups (0.279 vs 0.556) with a lesser statistical significance ($p=0.012$).

CONCLUSION

CSF-lactate level showed good discrimination value in identifying bacterial CSF infection in neurosurgical patients. Its potential can be further explored as a point of care test and may bring revolution to current standard of care.

Basic Neuro Science
OP_B_10

GENE REPLACEMENT THERAPY IN A SCHWANNOMAMOUSE MODEL OF NEUROFIBROMATOSIS TYPE 2

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INTRODUCTION

Loss of function of the neurofibromatosis type 2 (NF2) tumor suppressor gene leads to the formation of schwannomas, meningiomas, and ependymomas, comprising about 50% of all sporadic cases of primary nervous system tumors. NF2 syndrome is an autosomal dominant condition, with bi-allelic inactivation of germline and somatic alleles resulting in loss of function of the encoded protein merlin and activation of mammalian target of rapamycin (mTOR) pathway signaling in NF2deficient cells. Here we describe a gene replacement approach through direct intratumoral injection of an adeno-associated virus vector expressing merlin in a novel human schwannoma model in nude mice.

METHODS

In culture, the introduction of an AAV1 vector encoding merlin into CRISPR-modified human NF2- null arachnoidal cells (ACs) or Schwann cells (SCs) was associated with decreased size and mTORC1 pathway activation consistent with restored merlin activity. In vivo, a single injection of AAV1-merlin directly into human NF2-null SCderived tumors growing in the sciatic nerve of nude mice led to regression of tumors over a 10-week period, associated with a decrease in dividing cells and an increase in apoptosis, in comparison with vehicle.

RESULTS

Both in vitro and in vivo studies served as the proof of principle to restore merlin expression in NF2-deficient tumor cells for future potential to provide therapeutic efficacy. *In vitro*, we employed the AAV-based delivery of functional merlin to produce inhibition of mTORC1 activation in human NF2-null ACs and SCs cell lines. Further, we also established a new sciatic nerve xenograft model in nude mice for schwannomas using human NF2-null immortalized SCs for which a single intratumoral injection of the AAV-merlin vector with the aim to regress of tumor growth.

CONCLUSION

Our studies support suppression, and even regression, of human schwannoma growth in vivo by NF2 gene replacement in a preclinical xenograft mouse model. These studies establish that merlin reexpression via gene replacement in NF2-null schwannomas is sufficient to cause tumor regression, thereby potentially providing an effective treatment for NF2.

Basic Neuro Science
OP_B_11

EFFECTS OF IFENPRODIL ON PAIN BEHAVIOUR RESPONSES AND SPINAL APOPTOTIC REGULATION IN CFA-INDUCED CHRONIC POLYARTHRITIS MALE RATS

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory illness in which pain is frequently reported symptom. Ifenprodil, a selective N-methyl-D-aspartate receptor-2B (NMDAR-2B) antagonist, has been shown significant anti-nociceptive effect in neuropathic pain models. However, the effects of ifenprodil on pain, inflammatory markers, and apoptotic regulation have not been reported. The intent of this study aimed to investigate the effects of ifenprodil on pain behavioural responses, inflammatory parameters, and apoptotic markers in the spinal cord of CFA-induced chronic polyarthritis rats.

METHODS

CFA-induced arthritic rats received intrathecal treatment of either ifenprodil (0.5 or 1.0μg/μL) or sodium diclofenac (6μg/μL) (positive control) for 7 days. Pain behaviour assessments including tactile allodynia, thermal hyperalgesia, and spontaneous activities were conducted on day-0 (baseline), day-15 (pre-intervention) and day-23 (post-intervention). The lumbar region of the spinal cord (L4-L5) was collected for ELISA analysis, while histopathological examination was performed on ipsilateral ankle joint. Data was analysed by one-way ANOVA with post-hoc Bonferroni test. The significance level was taken at $p<0.05$.

RESULTS

The arthritic rats receiving ifenprodil (0.5μg/μL) showed increased paw and thermal withdrawal thresholds with reduced scoring of walking and standing paw pressures ($p<0.05$). Meanwhile, caspase-3, caspase-8, PKB, and PI3Kcb markers were decreased ($p<0.05$) with no change in Bcl-2 level in the spinal cord compared to the arthritis control group ($p<0.05$). There was a significant improvement in the morphology of the ipsilateral ankle joint compared to arthritis rat receiving ifenprodil at 1.0μg/μL.

CONCLUSION

Ifenprodil, especially at 0.5μg/μL, was found to be effective in suppressing arthritic pain responses, presumably through modulating the spinal cord apoptotic regulation with effects comparable to sodium diclofenac. These results reflect the significant contribution of NMDAR-2B in the pathogenesis of chronic arthritic pain.

Basic Neuro Science
PP_B_01

NEUROINFLAMMATION, A POTENTIAL MEDIATOR OF POST-TRAUMATIC SEIZURE & NEUROPSYCHIATRIC COMORBIDITIES IN A ZEBRAFISH MODEL OF TBI

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INTRODUCTION

Traumatic brain injury (TBI) causes lifelong and dynamic effects on one's health and well-being. Neuropsychiatric comorbidities and seizures are common adverse behavioral outcomes post-TBI, yet there is no effective treatment against them. We hypothesized that neuroinflammation could play a key role in the genesis of epilepsy and neuropsychiatric complications. The present study aimed to understand the role of neuroinflammation in TBI-induced spontaneous seizures and associated neuropsychiatric comorbidities.

METHODS

A weight-drop TBI induction model in zebrafish was used in the study. TBI group injuries were compared with the sham group. Post-traumatic (PTS) behaviors were recorded at day 0 and 12 post-injury. The PTZ-induced seizure was conducted, and daily seizure scores for 10 days were recorded. A novel tank test was utilized to assess anxiety, while a mirror bite test was used to for aggression. Gene expression analysis, proteomics, and neurotransmitter analysis were performed to evaluate the role of neuroinflammation.

RESULTS

Animals in the TBI group displayed delay in recovery compared to sham group. TBI animals also displayed a seizure score of 2 to 5 at 0 dpi, which persisted with a score of 2 to 4 at day 12 dpi. The TBI group also spent a long time in the bottom zone of the tank. Moreover, the TBI group also showed increased mirror biting frequency indicating aggression-like behavior. The seizure score of TBI zebrafish showed seizure score 4 as early as day 1 after PTZ injection, and the percentage of animals with seizures was statistically significant for seizure score 4 in TBI animals compared to sham. HMGB1, TLR4, and NFKB downregulation were observed in the TBI group from different time points, and Acetylcholine, GABA, and glutamate levels found to be low after 10 days of PTZ injection in the TBI group.

CONCLUSION

Our study depicted seizure activity with anxiety and aggression in TBI induced animals. Neuroinflammation might be contributing as a key precursor for TBI-associated seizures and neuropsychiatric comorbidities.

Basic Neuro Science
PP_B_02

EFFECT OF DAILY SUPPLEMENTATION OF TOCOTRIENOL-RICH FRACTION (TRF) ON THE BRAIN USING A MOUSE MODEL: A QUANTITATIVE PROTEOMICS APPROACH

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INTRODUCTION

Vitamin E is a known micronutrient that has been associated with antioxidant properties giving a neuroprotective effect in the brain. Palm oil is one of the major natural sources of tocotrienols found in the TRF. Palm TRF contains tocotrienols (70%) and tocopherols (30%). TRF is more cost-effective to produce, making it a better option to be promoted to the public as a health supplement. In addition, TRF contains a mixture of tocotrienols and tocopherols; which means that it could synergistically modulate the host immune system and exhibit neuroprotective effects. Even though many studies reported on TRF and its role as an anti-inflammatory, there is no empirical evidence of the proteome changes that take place in the brain following TFR supplementation. Thus, using a mouse model, this study is to uncover the effects of supplementation with a tocotrienol-rich fraction on the expression of proteins in the brain.

METHODS

The experimental mice were supplemented with TRF and soy oil (vehicle) through oral gavage for 12 weeks. The untreated mice were considered as control. Protein was extracted from the brain following the post-treatment, then label-free quantitative proteomic profiling was performed using the liquid chromatography-double mass spectrometry technique. TRF-treated brains identified differentially expressed proteins (DEP) were compared to untreated control and analyzed using bioinformatic databases for functional classification of proteins and pathway enrichment analysis.

RESULTS

A total of 43 DEP were identified from the proteome of the TRF-treated brain as compared to the untreated control and vehicle group. Bioinformatic analysis reveals that DEPs of TRF were able to modulate inflammation-mediated chemokine and cytokine signaling pathways. Our functional analysis demonstrated the DEP involved in key aspects of molecular function regulator, response to stimuli, developmental processes and metabolic processes.

CONCLUSION

The current findings suggest that TRF supplementation to modulate inflammationmediated chemokine and cytokine signaling pathways.

Basic Neuro Science
PP_B_03

COGNITIVE PERFORMANCE IN STROKE-PRONE SPONTANEOUSLY HYPERTENSIVE RATS: A HISTOLOGICAL ANALYSIS OF HIPPOCAMPUS

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INTRODUCTION

Cerebral small vessel disease (CSVD) refers to a condition where it affects the small vessels of the brain including capillaries, arterioles as well as venules in the brain. It leads to a progression of several cognitive impairments affecting the hippocampus, for example, Alzheimer's disease and dementia. It is asymptomatic at the early stage and only gets detected when it has progressed to the later stage due to the difficulty in viewing the small vessels *in vivo*. The detection of CSVD mainly depends on neuroimaging markers of the brain, which are white matter hyperintensities, microbleeds, lacunar infarcts, enlarged perivascular spaces, and brain atrophy. Histological studies of the hippocampus in identifying the pathological features of CSVD in animal models are important for a better understanding of the disease progression. Objective: This study aimed to identify the presence of histopathological features in the hippocampus of stroke-prone spontaneously hypertensive rats (SHRSP) from three different groups of age to correlate with the progression of CSVD. Hypothesis: It was hypothesized that all histopathological features, including microbleed, enlarged perivascular spaces, thick vessel wall, and hemosiderin deposition, are present in the hippocampus as well as the reduction in the thickness of the hippocampus of SHRSP rats.

METHODS

The SHRSP and Wistar Kyoto (WKY) rats were randomly assigned to three different age groups, i.e., 8 weeks, 14 weeks and 42 weeks. Their hippocampus was collected and subjected to Hematoxylin and Eosin (H&E) and Nissl staining, which then observed through a light microscope. H&E was used in detecting abnormalities and measuring hippocampus thickness, while Nissl staining was used for neuronal cell viability counting.

RESULTS

In both the SHRSP and WKY groups, none of the microbleeds and hemosiderin deposition was observed. However, all groups displayed larger perivascular spaces within their hippocampus. The only noticeable variation among the groups was in the thickness of their vessel walls, with the older group of SHRSP (42 weeks) showing the highest prevalence. The thickness of the hippocampal regions CA1, CA3, and DG showed insignificant differences among all groups. However, a notable finding emerged in the viability of CA3 neurons, particularly in the SHRSP group at 42 weeks of age, where a significantly higher level of cell viability was observed among other groups.

CONCLUSION

In conclusion, the absence of microbleeds and hemosiderin deposition in both the SHRSP and WKY groups, along with no significant difference in the hippocampus thickness, suggests that these factors may not directly contribute to the agedependent progression of CSVD. However, the intriguing finding of higher viability in CA3 neurons within the 42-week-old SHRSP group suggests a potential age-related association with CSVD, despite the expected neuronal loss, warranting further investigation.

Basic Neuro Science
PP_B_04

NANOTECHNOLOGY FOR SEIZURE MANAGEMENT: INVESTIGATING THE ANTI-CONVULSANT ACTIVITY OF EMBELIN-LOADED NANO LIPID CARRIERS IN A ZEBRAFISH LARVAE MODEL

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INTRODUCTION

Seizures are abnormal and unpredictable electrical activity in the brain which presents a great challenge in epilepsy management. Despite the availability of a range of antiseizure medications, about 1/3 of people with epilepsy still have inadequate and sideeffect free control, emphasizing the need for new efficacious and well-tolerated treatment. Embelin, derived from *Embelia ribes*, has garnered considerable interest in the field of epilepsy research due to its potential anti-convulsant activity. However, in order to achieve the full effect of Embelin, a safe and effective drug delivery system maybe crucial for its clinical translation. Thus, our study aims to formulate and investigate the anti-convulsant potential of a nano lipid carrier (NLCs)-embelin formulation using a zebrafish larvae model. Embelin was encapsulated in NLCs to enhance its solubility and bioavailability.

METHODS

The NLCs' optimal particle size, zeta potential, and encapsulation efficiency were characterized for nose-brain delivery. Next, the formulation toxicity was investigated using a zebrafish larvae model. Various parameters, including survival rate, swimming activity changes, and morphological alterations, were monitored following exposure to different concentrations of the embelin-loaded NLCs.

RESULTS

Preliminary results indicated that the embelin-loaded NLCs exhibited minimal toxicity, as evidenced by the absence of significant changes in survival rate and morphological abnormalities compared to the control group. Some changes in swimming activity were noticed which could indicate potential sedative/anti-convulsant activity, however this will be further verified using a seizure model. The current findings suggest the biocompatibility and potential safety of the embelin-loaded NLCs in the zebrafish larvae model.

CONCLUSION

Further investigations are warranted to explore the long-term toxicity effects and elucidate the potential anti-convulsant effects of embelin-loaded NLCs. Our study may pave the way for future applications of embelin as an anti-seizure medication as well as of nano-formulation as a drug delivery system in improving the efficacy of current medications.

Basic Neuro Science
PP_B_05

MORPHOMETRIC AND MOLECULAR CHARACTERIZATION OF DOWN SYNDROME HIPSC-DERIVED CEREBRAL ORGANOIDS

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INTRODUCTION

Trisomy 21 is the most common genetic cause of Down syndrome (DS) with an incidence of one out of every 800 live births. DS individuals have intellectual disabilities as well as various clinical manifestations throughout life. The molecular processes underlying the prenatal neurodevelopment of DS are poorly understood since it is challenging to harvest experimental materials directly from humans. Therefore, an *in vitro* 3D model of the human brain such as cerebral organoids can recapitulate the early neurodevelopment events, making them valuable for understanding DS brain development. This study examined morphometric growth and protein expression of cerebral organoids derived from three pairs of DS isogenic (disomic and trisomic) hiPSC lines.

METHODS

Cerebral organoids derived from DS human-iPSC lines were grown in mTESR® media and STEMdiff™ Cerebral Organoid Differentiation and Maturation kits. Micrographs of organoids were taken on *days-in vitro* (div) 1–7, 14, 21, 30, and 45. Image J was used to analyze the area, diameter, perimeter, and circularity of the organoids. Protein expression of TUJ1, DCX, NFIA, NESTIN, GFAP was analyzed by using Western blot method. All images were taken, and bands' intensities were analyzed using Image J software. Statistical differences between the disomic and trisomic DS parameters were compared and analyzed using GraphPad Prism version 9.0.

RESULTS

Overall, disomic cerebral organoids were greater in area and diameter than the trisomic group on day 46. Glial cell markers (NFIA) astrocytes (GFAP), neuro progenitor cells (NESTIN), and neuronal marker (TUJ1) were reduced in trisomic, whereas immature neurons (DCX) were increased in disomic cerebral organoids.

CONCLUSION

Our study shows that our *in vitro*-created 3D cerebral organoids from DS isogenic lines are potentially useful DS models to comprehend the fundamental of trisomy 21mediated DS in the prenatal development of DS individuals.

Basic Neuro Science
PP_B_06

CARDIAC ALTERATIONS IN PILOCARPINE-INDUCED RAT MODEL OF STATUS EPILEPTICUS

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INTRODUCTION

Status epilepticus (SE) is a life-threatening neurologic condition characterised by prolonged and repeated epileptic seizures. It requires immediate medical attention and poses a significant challenge that can be addressed with a reliable seizure prediction tool. Emerging evidence has described the correlation between seizures and disruptions in the autonomic nervous system (ANS), particularly cardiac features. This study aimed to investigate cardiac changes in the pilocarpine-induced SE in a rat model.

METHODS

Adult Sprague-Dawley rats were randomly assigned to two groups: pilocarpinetreated SE (n=5) and saline-treated control (n=4) groups for the study. Kaha Science rat telemeters were used for wireless electrocardiography (ECG) recording. Heart rate (HR) and heart rate variability (HRV) parameters during baseline measurement and the period before and after a seizure onset were analysed. The percentage change from baseline was calculated for these parameters and statistically analysed to compare the differences in ECG parameters between SE-induced and control groups.

RESULTS

All animals in the SE group reached stage 4-5 of the Racine's scale between 5-20 minutes after pilocarpine administration. HRV analysis revealed that prior to seizure onset, there is a significantly lower percentage change from baseline in the coefficient variation of RR intervals (CVRR) for the SE group compared to the control (-45.0% vs. 53.6%, $p<0.05$). Slightly lower percentage change from baseline in the standard deviation of RR intervals (SDRR) and root mean square of successive difference (RMSSD) were also observed before seizure onset in the SE group compared to the control, although the differences were not statistically significant.

CONCLUSION

The findings from this study indicate that there might be an imbalance between the parasympathetic and sympathetic branches of the ANS prior to seizure onset in the pilocarpine-induced rat model of status epilepticus. This study may provide insights into the development of seizure prediction tools based on cardiac abnormalities.

Basic Neuro Science
PP_B_07

KRATOM EXPOSURE DURING ADOLESCENCE DISRUPTS COGNITIVE BEHAVIOURS AND BRAIN METABOLITE PROFILES IN ADULT RATS

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INTRODUCTION

Exposure to drugs like opioids, psychostimulants and alcohol during adolescence can cause disruption in cognitive behaviours that persist into adulthood. Several studies have also shown that exposure to kratom (*M. speciosa* Korth) or its main alkaloid, mitragynine can cause various types of cognitive deficits. Hence, recreational kratom use among youth is very concerning as their brain is still developing and more vulnerable to the impact of early drug use.

OBJECTIVES

The present study aimed to investigate the effects of kratom exposure during adolescence on cognitive behaviours and brain metabolite profiles in adult rats.

METHODS

Adolescent male Sprague-Dawley rats (Postnatal day 31, PND31) were given vehicle, morphine, mitragynine (3, 10 or 30 mg/kg) or lyophilized kratom decoction (LKD, equivalent to 30 mg/kg of mitragynine) for 15 consecutive days. Animals were left undisturbed until they reached adulthood (PND70) and tested for a series of behavioural paradigms such as novel object recognition, social interaction and Morris water maze (MWM) tasks. 24 hours after behavioural testing, brains were harvested and LCMSbased metabolomic analysis was performed.

RESULTS

The results show that a high dose of mitragynine disrupted long-term recognition memory. Social behaviour and spatial learning were still intact but both mitragynine and LKD caused a deficit in reference memory of the MWM. Brain metabolomic analysis showed metabolic disturbances in arachidonic acid, taurine and hypotaurine, pantothenate and CoA, and tryptophan pathways. N-isovalerylglycine was identified as the potential biomarker.

CONCLUSION

These findings suggest that kratom exposure during adolescence can lead to lasting cognitive behavioural deficits and perturbation in brain metabolic pathways that are still evident in adulthood. The finding further suggests that the adolescent brain is susceptible to the impact of early kratom use.

Basic Neuro Science
PP_B_08

INTEGRATED ANALYSIS OF WGCNA AND MACHINE LEARNING IDENTIFIED CRITICAL BIOMARKERS IN DOWN SYNDROME BRAIN ORGANOIDS

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INTRODUCTION

Down syndrome (DS) is the most frequently diagnosed chromosomal disorder of chromosome 21 (HSA21) aneuploidy, characterized by intellectual disability and reduced lifespan. One of the DS hallmark features is a reduction in brain size and volume. The abnormal DS brain development is characterized by reduced neurogenesis and increased gliogenesis. The DS phenotypes may result from the interaction between the gene over-expressions mapping to trisomy HSA21 and subsequent dysregulation of genes mapping to different chromosomes.

METHODS

We downloaded sequencing data (training set: GSE222365 and testing set: PRJNA721827) for organoids from public databases. Differential expression analysis was performed using Galaxy web tools. The Weighted gene co-expression network analysis (WGCNA) was used to identify critical modules and genes highly associated with DS. Least absolute shrinkage and selection operator (LASSO) regression analysis, support vector machine (SVM), and random forest (RF) were performed to further screen critical differentially expressed genes (DEGs) in DS.

RESULTS

A total of 620 DEGs were obtained in the testing set. We identified 413 genes highly associated with DS using WGCNA. By taking the overlap between the WGCNA result and DEG, we got 109 crucial DEGs. Based on these genes, we screened 11 genes by LASSO regression analysis, 19 by SVM, and 10 by RF. PRMT2 and POFUT2 were obtained as essential genes by overlapping three algorithms. In the training set, we observed an upregulation of the expression levels of PRMT2 and POFUT2 and validated both in the testing set. In addition, by KEGG of gene co-expression analysis, we found that POFUT2 was associated with the Notch signaling pathway, and PRMT2 was associated with the JAK-STAT signaling pathway.

CONCLUSION

Our study revealed that PRMT2 and POFUT2 might be essential genes for abnormal brain development in DS, and they may serve as potential diagnostic biomarkers for DS and improve the understanding of its pathogenesis.

Basic Neuro Science
PP_B_09

EFFECTS OF PRENATAL RUXOLITINIB ON ASTROGLIOGENESIS VIA MODULATION OF THE JAK/STAT SIGNALING PATHWAY AND NEUROBEHAVIORAL ALTERATION IN MICE

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INTRODUCTION

Down syndrome (DS) is a well-recognized and common genetic disorder caused by triplication of human chromosome 21. Individuals with DS often exhibit reduced brain volume, an increased number of astrocytes, and a decreased number of neurons. These developmental brain morphogenetic changes are believed to be the underlying basis driving cognitive disabilities in DS. The neurogenic-to-gliogenic shift observed in DS brains is thought to be reversible by targeting the Janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling pathway, as JAK-STAT pathway plays a crucial role in promoting astrogenesis.

METHODS

C57BL/6 of pregnant mice were divided into two groups, control group (n=2) and treated group (n=3). At gestation 13.5, the control group (G1) and treated group (G2) were fed daily for seven days with 1% (w/v) methylcellulose in saline and 30 mg/kg body weight of ruxolitinib, respectively. The gene expression of Jak2, Stat3, the glial cells mRNA marker Gfap and S100b, as well as the mRNA neuron markers Tuj1 and NeuN, were assessed by the reverse transcription quantitative real-time PCR (RT-qPCR) in the postnatal day (P) 1.5 pup's brain from control (n=2) and treated group (n=3). The protein expression of pJak2 and Gfap, the critical markers for regulating astrogenesis, were determined by Western blot. The neurobehavioral changes in the adult mice (2-month-old, n=9) prenatally treated with ruxolitinib and control group (n=9) were then assessed using a battery of behavioral tests.

RESULTS

Treated ruxolitinib group (G2) showed no significant changes ($P<0.05$) compared to the untreated control group (G1) in all mRNA markers. Similarly, in the Western blot analysis, both protein markers for pJak2 and Gfap showed no significant differences between groups. Surprisingly, adult mice treated with ruxolitinib prenatally showed improvement in muscle strength. Moreover, the treated mice demonstrated a significant difference in escape latency during the training phase of the Morris water maze, indicating that the treated group exhibited improved learning capabilities compared to the control groups. However, no changes were observed in motor coordination, locomotor function, exploratory and anxiety-related behavior, recognition memory, or long-term memory.

CONCLUSION

Administration of ruxolitinib from E13.5 of pregnancy did not significantly suppress astrogenesis via the JAK/STAT signalling pathway, suggesting that alternative approaches or different time points of prenatal treatment may be necessary to achieve a notable reversal of the gliogenic shift in DS.

Basic Neuro Science
PP_B_10

GABAB RECEPTOR MODULATES REMYELINATION IN THE EXPERIMENTAL AUTOIMMUNE ENCEPHALITIS MODEL OF MULTIPLE SCLEROSIS

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INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system that is characterized by demyelination of the myelin sheath. Remyelination is a critical repair mechanism that can restore the function of damaged axons and improve clinical outcomes in MS patients. In this study, we investigate the role of GABAB receptor modulation in the context of remyelination in an experimental autoimmune encephalitis (EAE) animal model of MS which could have therapeutic implications for MS therapy.

METHODS

Postnatal rats 10 – 15 day were used in acute slices *in vitro* method and Sprague Dawley rats 4 – 8 weeks were immunized with MOG_{35-55} suspended in complete Freund's adjuvant (CFA) and pertussis toxin was used for *in vivo* study. The clinical symptoms (EAE score) and changes in body weight were assessed daily for 18 days, 21 days and 35 days.

RESULTS

To examine whether baclofen could affect the level of proliferation in acute spinal cord slices, the thymidine analogue 5-Ethynyl-2'-deoxyuridine (EdU) was added to the slices in the presence or absence of baclofen. The numbers of EdU-positive cells were significantly lower in baclofen-treated slices (p <0.05) compared with control EdUpositive cells in the central canal area. The daily weights and clinical scores in induced groups are statistically significantly different (p < 0.05). The Luxol fast blue stains white matter myelin, revealing the zone of demyelination 18 days after injection.

CONCLUSION

Our findings suggest that slices treated with baclofen had considerably fewer proliferative cells than control slices in the central canal area of the spinal cord and GABAB receptor antagonists might be able to initiate remyelination.

Basic Neuro Science
PP_B_11

TOXICOLOGICAL RISK ASSESSMENTS AND NEUROPROTECTIVE EFFECTS OF BAICALEIN-ENRICHED FRACTION ON ISCHEMIC STROKE RATS

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INTRODUCTION

In recent years, there has been growing evidence suggesting the potential of natural compounds derived from plants as a promising alternative strategy against ischemic stroke. One plant that shows promise in this regard is *Oroxylum indicum* which contains a potential neuroprotective compound known as baicalein. Baicalein is well known for its ability to cross the blood-brain barrier, making it a valuable therapeutic candidate for neurological diseases such as ischemic stroke. This study evaluated the safety and the therapeutic potential of baicalein extracted from the *O. indicum* leaves in the treatment of this disease.

METHODS

A binary solvent system was utilized to prepare baicalein-enriched fraction (BEF) from *O. indicum*. In this study, the safety profiles of BEF was assessed through acute and subacute neurotoxicity in preclinical models following the guidelines set by the Organization for Economic Co-operation and Development (OECD) Guidelines 420 and 424. Subsequently, 50 mg/kg BEF was given to rats for 4 days before the induction of ischemic stroke using endothelin 1 (ET-1).

RESULTS

No signs of treatment-related toxicity, neurotoxicological impairments, or alterations in hematological, biochemical and histopathological assessments in both acute and subacute neurotoxicity studies. It was also found that the BEF-treated ischemic stroke rats showed significantly improved neurological deficits, reduced brain infarct volume and lower histological scores of neuronal degradation, suggesting that consumption of BEF before the ischemic-stroke induction could provide substantial protection to brain tissue against the ischemic injury.

CONCLUSION

In summary, BEF exhibits potential as neuroprotective agent for enhancing clinical interventions in the treatment of ischemic stroke in the future.

Basic Neuro Science
PP_B_12

METABOLOMICS ANALYSIS OF THE NEUROPROTECTIVE EFFECT OF PERSICARIA MINOR EXTRACT IN CHRONIC CEREBRAL HYPOPERFUSED RATS

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INTRODUCTION

Persicaria minor (*P. minor*) is a herbal plant with many uses in food, perfume, and the medical industry. *P. minor* extract contains flavonoids with antioxidant and anticholinesterase capacity, which could enhance cognitive functions. *P. minor* extract has been proven to enhance memory. However, its role in an animal model of chronic cerebral hypoperfusion (CCH), which resembles human vascular dementia, has yet to be explored. Therefore, the present study investigates the effects of chronic administration of aqueous *P. minor* extract on different stages of learning and memory processes and the metabolic pathways involved in the chronic cerebral hypoperfused rats.

METHODS

Experimental CCH model was induced by permanent bilateral occlusion of common carotid arteries (PBOCCA) in rats. The effects of *P. minor* extract on motor and cognitive functions were evaluated using a series of behavioral tests. LC/MS-QTOF combined with computational analysis were used to determine differentially expressed metabolites and pathways involved.

RESULTS

Chronic treatment of *P. minor* extract at dose of 300 mg/kg, enhanced recognition memory of the PBOCCA rats. *P. minor* extract (300 mg/kg) was also found to restore the spatial memory impairment induced by CCH. Further, distinctive metabolite profiles were observed in rats with different treatments. Three major pathways involved in the cognitive enhancement mechanism of *P. minor* were identified.

CONCLUSION

The present findings demonstrated an improving effect of *P. minor* extract on memory in the CCH rat model, suggesting that *P. minor* extract could be a potential treatment for vascular dementia and Alzheimer's patients. *P. minor* is believed to improve cognitive deficits by regulating pathways involved in retinol, histidine, pentose, glucuronate, and CoA metabolism.

Basic Neuro Science
PP_B_13

ANTAGONISM OF THE GHRELIN RECEPTOR TYPE 1A INDUCES STATUS EPILEPTICUS IN THE ELECTRICAL KINDLING MODEL OF EPILEPSY

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INTRODUCTION
Ghrelin hormone exhibits anti-seizure properties in different models of epilepsy. Nevertheless, its effect has not been studied in the electrical kindling model of epilepsy. In this study, we evaluated the effect of antagonism of the ghrelin receptors in the brain of fully kindled rats.

METHODS
Adult male Wistar rats weighing 300 g were used. Animals were stereotaxically implanted with two monopolar electrodes in the skull surface, a tri-polar electrode in the basolateral amygdala, and a guide cannula in the left lateral ventricle. Animals underwent a semi-rapid kindling protocol. After showing three consecutive stages five seizures, the animals were considered fully kindled. A ghrelin antagonist (D-Lys-3GHRP-6) was injected intracerebroventricularly (icv) in the kindled animals at different dosages of 1, 50, and 100 μg/rat. Each rat was considered as its control. Seizure parameters including stage 4 latency (S4L), stage 5 duration (S5D), seizure stage (SS), and after discharge duration (ADD) were recorded.

RESULTS
Paired t-test indicated a significant increase ($p< 0.05$) in the seizure induction in the rapid kindled rats. D-lys-3-GHRP-6 (1 μg/rat; icv), significantly prolonged ADD in the kindled rats (30 second in control *vs* 37 second in treated). D-Lys-3-GHRP-6 injected at the dosages of 50, and 100 μg/rat; icv induced status epilepticus in the kindled rats.

CONCLUSION
The results indicate that antagonism of ghrelin functional receptors prolongs seizures and induces status epilepticus in the kindling model of epilepsy and propose that endogenous ghrelin has crucial antiepileptic properties.

Basic Neuro Science
PP_B_14

FRUITS: FOE OR FRIENDS FOR EPILEPSY

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INTRODUCTION

Epilepsy is a devastating neurological disorder where current anti-seizure medications are only effective in about 70% of patients, while the remaining are considered drugresistant. People with epilepsy are also concerned about what they consume, as some might provoke seizures. There is limited information available on fruits, especially which might provoke or prevent seizures. Phytochemicals in the fruits have been reported to have beneficial properties for seizures, such as anti-convulsant, antioxidant and anti-inflammatory activities. However, some fruits are also shown to have harmful effects in specific conditions.

METHODS

To understand more about fruits, a continuation of an experimental study from a previous systematic review have been carried out where we explored the commonly consumed fruits in South East Asia, including Malaysia, namely durian, mangosteen and rambutan on how they affect the outcome of epilepsy with the use of the zebrafish larvae model. Fruit extracts of these local fruits, mainly 50% and 95% Methanol and water were used for anti- and pro-convulsant analysis.

RESULTS

Some of these extracts were shown to lower the effects of the pentylenetetrazol (PTZ), a pro-convulsant used, while some of these extracts further increases the activity of PTZ. This shows that there are potential for both anti- and pro-convulsant activity among the fruit extracts used.

CONCLUSION

This study might be a guiding light for both people with epilepsy as well as carers to make an informed decision on which fruits to use and which to avoid.

Basic Neuro Science
PP_B_15

ORTHOSIPHON STAMINEUS STANDARDIZED EXTRACT REVERSES STREPTOZOTOCIN-INDUCED ALZHEIMER'S DISEASE-LIKE CONDITION IN A RAT MODEL

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INTRODUCTION

Alzheimer's disease (AD) is a chronic neurodegenerative brain disease that is characterized by impairment in cognitive functioning as well as the presence of intraneuronal neurofibrillary tangles (NFTs) and extracellular senile plaques. There is a growing interest in the potential of phytochemicals to improve memory, learning, and general cognitive abilities. The Malaysian herb
Orthosiphon stamineus is a traditional remedy that possesses anti-inflammatory, anti-oxidant, and free-radical scavenging abilities, all of which are known to protect against AD. Previous studies have reported that intracerebroventricular (ICV) administration of streptozotocin (STZ) mimics a condition similar to that observed in AD. This experiment thus aimed to explore if an ethanolic leaf extract of *O. stamineus* has the potential to be a novel treatment for AD in a rat model and can reverse the STZ- induced learning and memory dysfunction.

METHODS

Administration of STZ via the intracerebroventricular (ICV) route is a reliable model resembling sporadic AD (SAD) associated neuropathological changes. In this study, ICV-STZ (3 mg/kg) was injected once bilaterally into male Sprague Dawley rats, followed by daily administration of *O. stamineus* (orally, 50, 100 & 200 mg/kg) for 10 days. Cognitive functions were evaluated by elevated plus maze test (EPM) and passive avoidance test (PA). The pharmacological activity of *O. stamineus* was further assessed through the expression levels of amyloid precursor protein (APP), microtubule-associated protein tau (MAPT), nuclear factor kappa-light-chainenhancer of activated B (NFκB), glycogen synthase kinase-3 alpha (GSK3-α), and glycogen synthase kinase 3 beta (GSK3-β) genes, which are key genes that are undeniably crucial in comprehending the pathogenesis of AD.

RESULTS

The results of this study indicate that *O. stamineus* has the potential to be potentially effective against AD-like condition, as both behavioral models employed in this study was observed to be able to reverse memory impairment. Treatment with the extract was able to decrease the up-regulated expression levels of amyloid precursor protein (APP), microtubule associated protein tau (MAPT), Nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB), glycogen synthase kinase 3 alpha (GSK3α), and glycogen synthase kinase 3 beta (GSK3β) genes indicating the extract's neuroprotective ability.

CONCLUSION

These research findings suggest that the *O. stamineus* ethanolic extract demonstrated an improved effect on memory, and hence, could serve as a potential therapeutic target for the treatment of neurodegenerative diseases such as AD.

Basic Neuro Science
PP_B_16

REST AND SYNAPTIC DEVELOPMENT GENE & PROTEIN EXPRESSIONS IN DOWN SYNDROME IPSC-DERIVED CEREBRAL ORGANOIDS

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INTRODUCTION

Down syndrome (DS) is a genetic developmental disorder caused by trisomy of the human chromosome 21. Complex neuropathology is always reported in DS including deficit neurogenesis and impaired synaptic developments. These impairments lead to loss of efficient neurotransmission and contribute to DS intellectual disabilities. Repressor Element-1 Silencing Transcription Factor (REST) is a key epigenetic neuronal gene repressor. REST is downregulated and loses its function in DS. However, the association between REST dysregulation and DS synaptic impairments remained unknown. Hence, this study aimed to profile the REST and its target synaptic genes expressions (i.e., Synapsin1, Synaptophysin, PSD-95, MAP2, Drebrin, and VGLUT2) in DS cerebral organoids (COs).

METHODS

Isogenic (disomic control and trisomic DS) human-induced pluripotent stem cells (hiPSCs) were derived into COs (*n=2*) and harvested at 45 days-in-vitro (div). Next, qPCR and Western blot (WB) were performed to measure the gene and protein expressions. Paired t-test was applied for statistical analysis.

RESULTS

The qPCR results showed that REST and all synaptic genes were not significantly different between isogenic CO pairs. Fascinatingly, the pre-synaptic marker expressions in WB were significantly increased in trisomic DS compared to the disomic control. This finding is aligned with the DS early developmental neuropathology - accelerated neuron maturation. DS then produces non-functional premature neurons which depletes the compensating neural stem cell pool and leads to accelerated ageing. Nevertheless, REST is not downregulated in DS COs potentially due to incomplete COs' neuronal development at div-46. Characterization with an extended *div-3-month* COs is required as functional excitatory neurons were reported.

CONCLUSION

This study showed that pre-synaptic markers were significantly upregulated in trisomic DS cerebral organoids, and this supports the DS accelerated neuron maturation. Further characterization of REST epigenetic binding and repression effects on target synaptic genes is needed to reveal the association between REST dysregulation and DS synaptic impairments.

Basic Neuro Science
PP_B_17

NEUROINFLAMMATION, A COMMON PATHWAY IN ALZHEIMER'S DISEASE AND EPILEPSY: A SYSTEMATIC REVIEW

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INTRODUCTION

Neuroinflammation is a key pathological response of the central nervous system that may be induced by a brain insult, and is often seen as a precursor in neurodegenerative conditions. Recent research has shown that neuroinflammation may contribute to the initiation of Alzheimer's disease (AD) pathogenesis as well as in epileptogenesis. About 64% of people with AD have epileptic seizures as a co-morbid condition. This systematic review aimed to summarise the shared molecular mechanisms of neuroinflammation in both AD and epilepsy.

METHODS

A literature search was performed on reputable databases such as PubMed, Ovid Medline, Scopus, and EMBASE. Search terms such as neuroinflammation, Alzheimer's disease, epilepsy, seizure and cognitive decline were utilized. A total of 2760 articles were screened according to the inclusion and exclusion criteria. English, full text original research articles related to the modulation of the inflammatory biomarkers commonly associated with the progression of AD and epilepsy in all populations were included in this review.

RESULTS

Only 7 articles met the inclusion criteria and were chosen for further analysis. Selected studies included both *in vitro* and *in vivo* studies. Due to the diverse nature of the data and data analyses, a meta-analysis was not performed. Several neuroinflammatory biomarkers were reported to be involved in the crosstalk between AD and epilepsy which are glial fibrillary acidic protein (GFAP), ionised calcium-binding adaptor molecule 1 (Iba1), interleukin 1-beta (IL-1β) and tumour necrosis factor-alpha (TNF- α).

CONCLUSION

Neuroinflammation was directly associated with the advancement of AD to epilepsy. However, there is a need for more reproducible studies focusing on the common inflammatory biomarkers to develop standardised monitoring guidelines to prevent the manifestation of epilepsy in patients with AD.

Basic Neuro Science
PP_B_18

EVALUATION OF PHARMACOGNOSTIC, PHYTOCHEMICAL AND NEUROPROTECTIVE PROPERTIES OF BAICALEIN-ENRICHED FRACTION EXTRACTED FROM OROXYLUM INDICUM

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INTRODUCTION

Oroxylum indicum is a widely distributed medicinal plant in Southeast Asia that exhibits extensive therapeutic values. One of the key compounds that responsible for *O. indicum* biological activities is baicalein. Baicalein is well known for its neuroprotective and anti-oxidant properties, making it a potential therapeutic agent for ischemic stroke disease. This study focused on the investigation of pharmacognostic, phytochemical and neuroprotective properties of baicaleinenriched fraction (BEF) extracted from *O. indicum*.

METHODS

The pharmacognostic features of *O. indicum* leaves was evaluated using macroscopic, microscopic and physicochemical analysis prior to the extraction of BEF. Characterization of the BEF was performed using phytochemical analysis, fourier transform infrared spectrophotometer (FTIR), and high-performance liquid chromatography (HPLC) assays. The neuroprotective effects of BEF on neural stem cell gene expression also were investigated using real-time PCR.

RESULTS

Physicochemical analysis of the *O. indicum* leaves powder showed total-ash, watersoluble ash, and acid-insoluble values of 8.66, 6.14, and 0.059 %w/w, respectively. Transverse section of the leaf showed well-developed upper and lower epidermis covered by cuticle and made up of thin-walled rectangular cells. Phytochemical analysis revealed the presence of phenol, tannins, phlobatannin, flavonoid, saponin, quinines, and glycosides. FTIR spectroscopy identified phenol, hydroxyl and carbonyl as the major functional groups while HPLC analysis revealed that the extract contained 29% of baicalein. Moreover, NSCs treated with 3.125 µg/ml of BEF for 48 hours showed significant upregulation of superoxide dismutase (SOD2, 3.38-fold) and angiopoietin (ANGPT1, 6.24-fold) genes, compared to non-treated NSCs.

CONCLUSION

In conclusion, this study presented the pharmacognostic and phytochemical parameters that are necessary for the identification of the *O. indicum* plant and a new doorstep to find out any adulteration in the plant. Most importantly, this study also confirmed the neuroprotective effects of BEF extracted from *O. indicum* where it will serve as basis data for the development of potential ischemic stroke treatment.

Basic Neuro Science
PP_B_19

MINOCYCLINE IMPROVES NEUROPATHIC PAIN BEHAVIOR AND SCIATIC NERVE HISTOLOGY CHANGES IN DIABETIC TYPE 2 RAT'S MODEL.

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INTRODUCTION
The aim of this study was to determine the effects of minocycline (glial cell activation) and gabapentin on neuropathic pain behavior and sciatic nerve histological changes in diabetic type 2 rat's model.

METHODS
Male Sprague Dawley rats were randomly assigned to one of six groups (n=16 per groups): control (C), diabetic (STZ), diabetic treated with minocycline 40 mg/kg (STZ+ M40) and 80 mg/kg (STZ + M80), diabetic treated with gabapentin (STZ + G10) and non PDN (NPDN). Diabetic type 2 was induced in rats using a high fat diet (HFD) and low dose streptozotocin injection (i.p). The rats were sacrificed after neuropathic pain behaviour, body weight and fasting blood glucose (FBG) level measurements. The sciatic nerve was collected for histological examination.

RESULTS
At week 6, all HFD-treated groups were significantly heavier than the control groups. There was a significant increase in FBG levels in all diabetes groups on day 3, day 14, and day 22 of the study ($p<0.05$). The duration of paw licking or jumping was significantly reduced in the STZ+M40 and STZ+M80 groups on day 14 when compared to the control group ($p<0.05$). STZ administered caused significant histopathological changes in the sciatic nerve, but the numbers of degenerated sciatic nerve were reduced in rats given higher doses of minocycline and gabapentin.

CONCLUSION
High dose minocycline treatment was found to reduce neuropathic pain behavior and sciatic nerve histology changes. These findings highlight neuroprotective strategies and potential therapeutic targets for diabetes related PDN management.

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EFFECTS OF FORMULATED KRATOM DECOCTION AND FORMULATED MITRAGYNINE FROM *MITRAGYNA SPECIOSA* LEAVES ON THE HIPPOCAMPAL SYNAPTIC PLASTICITY IN RATS

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INTRODUCTION

Mitragyna speciosa (*M. speciosa*) Korth, also known as kratom or biak-biak, belongs to the family of Rubiaceae and its major indole alkaloid, mitragynine which has been used as a recreational drug and 'herbal high' preparation in the Southeast Asia and Western countries. Kratom leaves have been used as a treatment for pain management and opioid withdrawal. Many scientific studies have shown that mitragynine possesses abuse liability with impaired cognitive functions. However, no scientific evidence of formulated kratom decoction and mitragynine on the hippocampal synaptic plasticity has been carried out. Therefore, it has prompted us to investigate the effects of formulated kratom decoction and formulated mitragynine from the leaves of *M. speciosa* on the hippocampal synaptic plasticity in rats.

METHODS

The kratom decoction was prepared from the fresh leaves of *M. speciosa* by using the boiling technique. The dried kratom decoction or mitragynine powder was mixed with melted gelucire (14/44), followed by constant stirring for 30 minutes. The rats were divided into six groups of treatment: control (20% Tween 20); control (gelucire); formulated kratom decoction 500mg/kg; formulated mitragynine 10mg/kg; nonformulated kratom decoction (500mg/kg); non-formulated mitragynine (10mg/kg). The dose of kratom decoction (500 mg/kg) is equivalent to 10mg/kg mitragynine. The *in vivo* hippocampal synaptic plasticity was recorded contralaterally at CA3-CA1 regions using electrophysiological recording technique.

RESULTS

Single administration of all treated groups: both formulated and non-formulated kratom decoction (500 mg/kg) and mitragynine (10 mg/kg) suppressed the fEPSP amplitude significantly compared to control rats that treated with 20% Tween 20 or gelucire. Following two hours of recording, rats that received both kratom decoction (formulated and non-formulated) and mitragynine (formulated and non-formulated) significantly inhibited hippocampal synaptic plasticity when compared to control groups. However, no significant effect was observed in the short-term synaptic plasticity following the administration of kratom decoction and mitragynine (formulated and non-formulated).

CONCLUSION

Our findings suggest that formulated kratom decoction and mitragynine from the leaves of *M. speciosa* significantly caused hippocampal synaptic plasticity impairment. Hence, this dose of formulated kratom decoction has the potential to cause cognitive decline.

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DISCOVERING THE GLOBAL LANDSCAPE OF KNEE OSTEOARTHRITIS AND PAIN MANAGEMENT: A BIBLIOMETRIC ANALYSIS

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INTRODUCTION

Given the rapid growth of the global aging population, knee osteoarthritis (OA) has become an unneglectable concern amongst the elderly. The amount of published scientific research on knee OA and pain management has increased over time, but few studies have utilized bibliometrics in analyzing scientific research in this field. The purpose of this study is to conduct a bibliometric analysis of the literature on knee OA and pain management, with a visualization of trends that were published between 1998 to 2022.

METHODS

Knee OA and pain management were used as keywords to screen article titles from the Scopus database on November 11, 2022. A total of 859 documents were subjected to frequency analysis using Microsoft Excel, data visualization via VOSviewer, and citation metrics and analysis using Harzing's Publish or Perish.

RESULTS

Publications on knee OA and pain management demonstrated an increasing trend since 1998, consistent with this study's findings. The United States of America (USA) ranked first in research activity on knee OA and pain management. Furthermore,160 scholars from 73 countries and 160 institutions published related articles in different languages with multiple authors. The most cited article was "Effectiveness of Non-Steroidal Anti-Inflammatory Drugs for the Treatment of Pain in Knee and Hip Osteoarthritis: A Network Meta-Analysis" by da Costa et al. The journals with the most publications on knee OA and pain management were BMC Musculoskeletal Disorders (n=40), Osteoarthritis and Cartilage (n=30), and BMJ Open (n=27). The top 3 institutions by publication number were the University of Sydney (n=29), the University of Melbourne (n=26), and Harvard Medical School (n=22).

CONCLUSION

This work provides researchers with an in-depth understanding of knee OA pain management by evaluating relevant publications in the past two decades. Future research should further explore pain management in knee OA patients and the underlying mechanisms of pain.

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ANALGESIC POTENTIAL OF *MELALEUCA CAJUPUTI POWELL* ESSENTIAL OIL

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INTRODUCTION

Knee osteoarthritis (KOA) is a progressive degenerative disease characterized by destruction of articular cartilage leading years of living with functional disability. Malaysia is estimated to have an escalating number of KOA patients due to ageing population and resilience of obesity. Current management of KOA focuses on reducing pain and delaying the cartilage loss such as giving the nonsteroidal anti-inflammatory medications (NSAIDs), intra-articular corticosteroid or hyaluronic injection and surgical methods. However, there are currently no effective preventive or curative pharmaceutical treatments for KOA calling upon complementary medicine to curb its unpleasant sensation of pain. Hence, this study aimed to measure the anti-inflammatory properties bestowed in *Melaleuca cajuputi Powell*, a Malaysian tea tree essential oil (EO) and its pain reduction capacity towards KOA patients.

METHOD

Gas chromatography flame ionization detector (GC-FID) and gas chromatography mass spectrometry (GC-MS) analysis were performed to identify the anti-inflammatory components presents in this EO. A grade-IV KOA patient was recruited to evaluate his pain level using verbal report of Numerical Rating Score (NRS). Pain levels were measured during resting, during activities-induced pain and after EO application.

RESULTS A total of 34 compounds were found in the *M. cajuput Powell* essential oil, classified into four groups: monoterpene, monoterpenoid, sesquiterpene and sesquiterpenoid. 90.93 percents of its composition are attributable to anti-inflammatory activities such as beta-caryophyllene which exerts its effect by attenuating pro-inflammatory cytokines and inflammatory mediators of COX-2 and iNOS. Results from NRS showed that pain severity level was at grade 4 during resting condition, escalated to grade 9 during pain induced activities but shrank immediately to grade 4 after EO application.

CONCLUSION

Based on the gas chromatography analysis and patient's verbal report, *Melaleuca cajuputi Powell* EO appears to reduce KOA pain due to its anti-inflammatory activities.

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