Washington University
School of Medicine
Department of Neurology

Residents' Day Symposium
Friday, May 22, 2015
7:30am – 9:15am
Farrell Learning and Teaching Center ~ Atrium

Poster presentations will begin at 7:30am

Awards will be presented at 9:00am

We encourage everyone to attend this important event.

Adderley, Mark; Jain, Abhishaik; Grover, Prateek; and Malik, Ikram (Ike)

Anti-NMDA Receptor Encephalitis - A Case Report

Abstract: A 20 y.o. AA/ Caucasian female presented with paresthesias and weakness in both legs. She had a wtinessed event at home of shaking in extensor posture. EEG and HCT were unremarkable and the patient was discharged home on Keppra. Subsequently, the patient displayed sexually inappropriate behavior, hallucinations, and became agitated. She was admitted to psychiatry where she became progressively somnolent and further workup was warranted. MRI/MRA proved unremarkable and repeat EEG showed delta-slowing. LP showed lymphocytosis and anti-NMDAR antibodies. Clinically she displayed sympathetic surges, orofacial dyskinesias, and episodes of limb rigidity.

Anderson, Jacquie

Utility of Repeat Surveillance Neuroimaging for Cerebral Arteriovenous Malformations in Children with Hereditary Hemorrhagic Telangiectasia

Abstract: Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant disorder of angiogenesis leading to epistaxis, mucocutaneous telangiectases, and arteriovenous malformations. Children with HHT are susceptible to unexpected complications of cerebral arteriovenous malformations (CAVM's) including hemorrhagic stroke. Current international guidelines recommend a single brain MRI in the first 6 months of life or at diagnosis. There are no published reports of a pediatric patient developing new CAVM after initial brain MRI, and no data exist to guide timing of repeat surveillance neuroimaging. We report our experience with 36 pediatric patients over 13 years in a single referral center.

Baldassari, Laura

Modified EDSS within Multiple Sclerosis Clinical Practice

Laura E. Baldassari, MD, MHS; Erin Longbrake, MD, PhD; Anne H. Cross, MD; Robert T. Naismith, MD

Objective: Expanded Disability Status Scale (EDSS) is the standard research measure of disability in multiple sclerosis (MS). Limitations for clinical use include time required, scoring complexity, and technique redundancy. If simplified, the EDSS would provide a valuable numerical rating to monitor disease progression and treatment response. We developed a modified version of the EDSS (mEDSS), more conducive to clinical use, with comparisons to the full EDSS.

Methods: Consensus among 3 MS specialists was reached for a more concise EDSS, reflecting exam techniques utilized for clinical monitoring. The two scores were compared by a retrospective chart review (n=102). Spearman's rank correlation coefficients and Bland-Altman plots were assessed. Reasons for discordant scores were delineated.

Results: The mEDSS had strong correlation with the EDSS, both overall (Spearman's rho = 0.99 (95% CI 0.94 to 0.97, $p<0.001$)) and for each functional system (Spearman's rho between 0.90 and 1.00, p-values <0.001). Correlations were consistent across the spectrum of disease.

Conclusions: The mEDSS can be performed within 5 minutes, was strongly correlated with the full EDSS, and can provide a useful rating for disability in clinical practice. Longitudinal assessment of the mEDSS for stability and relapse sensitivity are in progress.

Burford, Matthew

Etiology and complications of Guillain-Barre Syndrome: An Illustrative Case

Introduction: Guillain-Barre Syndrome (GBS) is the most common cause of acute, flaccid paralysis since Poliomyelitis has been effectively eradicated through public health initiatives. There is much research suggesting a molecular mimicry physiology between lipooligosaccharide structures of Campylobactor jejuni and anti-ganglioside antibodies that cause disease. This close connection, however, is most strongly seen in cases of acute axonal forms of GBS that are predominant in Asia, but represent only a small minority of cases in the many Western nations.

In the United States, majority of GBS is of the demyelinating variant that is usually not associated with anti-ganglioside antibodies, making the pathogenesis of the disease unclear. In addition to bacterial infections, GBS has also been associated with preceding viral infections, particularly cytomegalovirus (CMV). While CMV-related GBS remains a minority of cases (10-15%), there are distinctive features to these cases that may help to identify a specific pathophysiology. This case illustrates a number of the distinctive features of CMV-related GBS as well as a rare complication that can be seen in GBS.

Case Description: A 36 year old woman presents with progressive weakness for 1 week and is found to have CMV viremia.

Clinical Course: After being admitted to the hospital with a diagnosis of GBS, she is treated with IVIg to hasten recovery. After receiving IVIg and in the setting of new hypertension, she develops signs symptoms consistent with reversible posterior leukoencephalopathy (RPLE), which is confirmed on imaging. She is transferred to our facility for further care where a persistent transaminitis and particularly prominent facial diplegia prompt testing for CMV, revealing active viremia. She is initiated on antiviral treatment. Her limb strength improves over weeks, but even 1 year out, she continues to have some facial weakness.

Conclusion: Guillain-Barre Syndrome likely represents several disparate but connected disease entities. This case illustrates some of the characteristic features of a specific form of demyelinating GBS. New research suggests that there may be novel antibodies to moesin that could be involved in the pathophysiology of CMV-related GBS and may have implications in the new treatment strategies for GBS in the United States.

Curfman, David

Ischemic and Hemorrhagic Cerebrovascular Events after Left Ventricular Assist Devices

Pouya Tahsili-Fahadan, MD, PhD, David R Curfman, MD, Albert A Davis, MD, PhD, Noushin Yahyavi-Firouz-Abadi, MD, Michael E Nassif, PhD, Shane J LaRue, MD, Gregory A Ewald, MD, Allyson R Zazulia, MD

Introduction: Left ventricular assist devices (LVADs) are mechanical circulatory support devices increasingly implanted for advanced heart failure either as a bridge to transplantation (BTT) or destination therapy (DT). The reported incidence of cerebrovascular events (CVEs) following LVAD is 8-25%. The effects of medical comorbidities and perioperative events on the development of CVEs are unclear.

Methods: 71 patients (19%) with CVEs were retrospectively identified from the Barnes-Jewish Hospital LVAD database (n=373; Heartmate II 87%, Heartware 13%) from 05/2005-12/2013. Demographic, clinical and outcome data were collected and analyzed in patients with and without CVEs using standard statistical methods.

Results: Coronary artery disease (P=0.007), diabetes mellitus (P=0.02) and LVAD indication of DT (P=0.04) were more common in patients with CVEs. Duration of cardiopulmonary bypass, hospital length of stay or incidence of bacteremia were not different between those with early CVE (within 30 days of implantation, 35%) and without CVEs. CVEs were ischemic (ICVE) in 35 (49%), hemorrhagic (HCVE) in 26 (37%), and ischemic + hemorrhagic in 10 (14%). ICVEs and HCVEs did not differ in demographic variables, pre-LVAD co-morbidities, post-LVAD complications, or NIH Stroke Scale at the time of event. In patients with no anti-thrombotic regimen (ATR) only ICVEs occurred. Among other 12 ATRs at the time of CVE, with aspirin+warfarin being the most common, no difference was found between ICVEs and HCVEs. Patients with HCVEs were more likely to be discharged with no ATR (P=0.015). Mortality was significantly higher in patients with CVE (59.1% vs. 29.2% in those without CVE) but did not differ by CVE type. In patients with CVE, 57.1% of deaths were secondary to the CVE (ICVE 25%, HCVE 93.7%, P<0.001). Among BTT patients, only 14.6% of patients with CVE underwent transplantation vs. 39.8% of patients without CVE (P =0.002).

Conclusions: LVADs are associated with high rates of ICVEs and HCVEs. In addition, CVEs are associated with increased mortality and lower rates of heart transplantation. Further investigations to identify risk factors for CVEs in post-LVAD patients and potential preventive measures including optimal ATRs are warranted.

Davis, Albert (Gus)

Variants in *GBA*, *SNCA,* and *MAPT* Influence Parkinson Disease Risk, Age at Onset, and Progression

Albert A. Davis[a], Kristin G. Andruska[a], Bruno A. Benitez[b], Brad A. Racette[a,f,g], Joel S. Perlmutter[a,c,d,e,f], and Carlos Cruchaga[b,f]

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Abstract: Multiple genetic variants have been linked to risk of Parkinson disease (PD), but known mutations do not explain a large proportion of the total PD cases. Similarly, multiple loci have been associated with PD risk by Genome-Wide Association Studies (GWAS). The influence that genetic factors confer upon phenotypic diversity remains unclear. Few studies have been performed to determine whether the GWAS loci are also associated with age at onset (AAO) or motor progression. We used two PD case-control datasets (Washington University and the Parkinson's Progression Markers Initiative) to determine whether polymorphisms located at the GWAS top hits (*GBA*, *ACMSD/TMEM163*, *STK39*, *MCCC1/LAMP3*, *GAK/TMEM175*, *SNCA*, and *MAPT*) show association with AAO or motor progression. We found associations between SNPs at the *GBA* and *MAPT* loci and PD AAO and progression. These findings reinforce the complex genetic basis of PD and suggest that distinct genes and variants explain the genetic architecture of PD risk, onset, and progression.

Dietz, Alexander

Nerve Ultrasound Identifies Abnormalities in the Posterior Interosseous Nerve in Patients with Proximal Radial Neuropathies

Introduction: The radial and posterior interosseous nerves (PIN) are prone to injury at multiple sites. Electrodiagnosis identifies the most proximal lesion. Nerve ultrasound could augment electrodiagnosis by visualizing additional pathology.

Methods: Retrospective examination of ultrasound and electrodiagnosis from 27 patients evaluated for posterior cord/radial/PIN lesions.

Results: 19/27 patients had abnormalities on electrodiagnosis (16 radial; 2 PIN; 1 posterior cord). Ultrasound confirmed electrodiagnostic abnormalities in 16/19 (84%). Ultrasound provided additional diagnostic information. In 6/16 (38%) patients with electrodiagnostic evidence of radial neuropathy, ultrasound identified both radial nerve enlargement and additional, unsuspected PIN enlargement (53% to 339% enlarged vs. unaffected side). Ultrasound also identified: Nerve (dis)continuity at the trauma site (n=8); and Nerve tumor (n=2; 1 with normal electrodiagnostics).

Conclusion: In radial neuropathy, ultrasound often augments electrodiagnosis and identifies a second pathology in the PIN. Further studies are required to determine the etiology and significance of this additional distal pathology.

Fay, Alex and Meddles, Katherine (Kit)

HIV-related Cognitive Difficulty in Vertically Transmitted HIV in Myanmar

Objective: To determine the impact of perinatally acquired HIV on specific neurocognitive domains in Myanmar children on antiretroviral therapy by comparison to a sample of seronegative children with optimal control over demographic variables.

Background: The majority of neurocognitive studies in HIV-infected children have been performed in the United States and Europe. Studies from resource-poor countries have shown that HIV-infected children differ in socioeconomic, nutritional and caregiver status compared to normal controls. Myanmar has one of the highest HIV-1 prevalence rates in Southeast Asia. Some vertically-infected orphaned children reside separately from HIV-negative children in separate orphanages, thus the demographic variables of interest are naturally controlled. We hypothesized that HIV-infected orphans would perform significantly worse on cognitive indices compared to HIV-negative orphans.

Design/Methods: A battery of cognitive tests sensitive to HIV-associated deficits in children was administered to 28 perinatally-acquired HIV-infected children and 31 HIV negative children (6 to 16 years old) from two orphanages in Yangon, Myanmar.
Results: Comparison of groups using independent t-tests indicates that the HIV-infected children perform more poorly than HIV-negative children across all tests, with significant group differences observed on assessments of executive function, visuospatial reasoning, fine motor dexterity, and visual motor integration.

Conclusions: Our results demonstrate a strong effect of HIV on specific neurocognitive deficits in vertically infected children. Understanding the viral and host determinants, timing of the treatment, and the choice of ART on cognition will be critically important in the treatment of HIV in children to prevent cognitive impairment of surviving children.

Kang, Peter

Blood Burden Mediates the Association between Bleeding Pattern and Hydrocephalus in Nonaneurysmal Subarachnoid Hemorrhage

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Introduction: Hydrocephalus requiring external ventricular drain (EVD) or shunt placement commonly complicates aneurysmal subarachnoid hemorrhage (SAH) but its frequency is not as well known for nonaneurysmal SAH (NA-SAH). Those with diffuse bleeding may have greater risk of hydrocephalus than those with a perimesencephalic pattern. We evaluated the frequency of hydrocephalus in NA-SAH and whether imaging factors could predict the need for EVD and shunting. We specifically investigated whether the previously demonstrated relationship between bleeding pattern and hydrocephalus was mediated through total blood burden.

Methods: We collected admission clinical and imaging variables for 105 NA-SAH patients, including bicaudate index (BI), Hijdra sum score (HSS), intraventricular hemorrhage (IVH) score, modified Fisher scale (mFS), and bleeding pattern. Hydrocephalus was categorized as acute (need for EVD) or chronic (shunt). We applied logistic regression to determine whether hydrocephalus risk was independently related to bleeding pattern or mediated through blood volume or ventriculomegaly.

Results: Acute hydrocephalus was seen in 26 (25%) patients but was more common with diffuse (15/28, 54%) versus perimesencephalic (10/59, 17%, $p<0.001$) bleeding. Patients developing acute hydrocephalus had worse clinical grade and higher BI, HSS and IVH scores. Patients with diffuse bleeding also had higher BI and HSS. Adjusting the relationship between acute hydrocephalus and diffuse bleeding for HSS, but not BI, nullified this association. Overall, 10 (9.5%) patients developed chronic hydrocephalus. Adjusting the relationship of chronic hydrocephalus and diffuse bleeding in the entire cohort for HSS and BI both nullified this association.

Conclusion: NA-SAH patients are at risk for acute hydrocephalus at 25% and chronic hydrocephalus at 10%. The greater risk in diffuse bleeding appears to be mediated by greater cisternal blood volume but not by greater ventriculomegaly in acute hydrocephalus and both greater cisternal blood and ventriculomegaly in chronic hydrocephalus. Imaging characteristics may aid in anticipatory management of hydrocephalus in NA-SAH.

Conflict of Interest Statement: The authors declare they have no conflict of interest related to the current study.

Kung, Nathan

Intravascular T-cell Lymphoma of the CNS

Abstract: A 59 year-old woman presented to our institution with three works of progressive speaking difficulties. MRI showed diffuse leptomeningeal enhancement and progressive cerebral infarctions. She initially responded to IV Methylprednisolone but eventually developed cerebral edema and herniated. In our poster we will show interesting images of Intravascular Lymphoma on MRI and on pathology and discuss the diagnostic difficulties of IVL.

Landsness, Eric

Use of Ziprasidone as a Treatment for Status Migrainosus at Barnes-Jewish Hospital

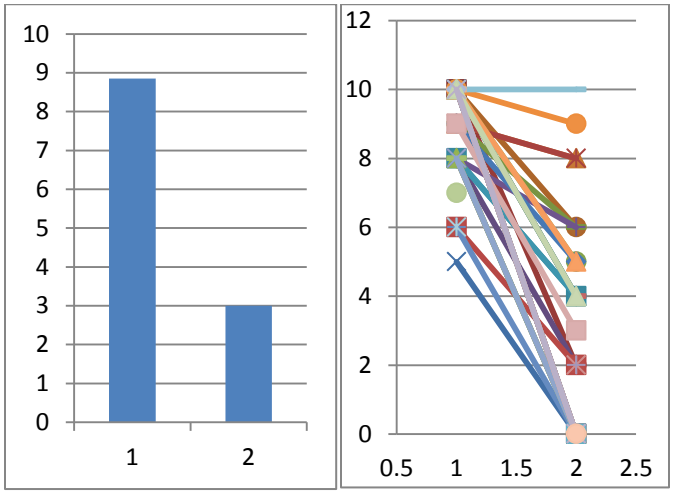
Eric C. Landsness, MD, Robert C. Bucelli, MD, PhD

Background: Migraine headache is one of the most prevalent neurologic disorders. Status migrainosus often results in admission to the hospital for abortive therapies. Often multiple medications are required for symptomatic relief. In 2007 neurologists at Barnes-Jewish Hospital began using the atypical antipsychotic ziprasidone as an abortive medication for status migrainosus. To date there are no published reports of this off-label use of ziprasidone.

Methods: The Clinical Investigation Data Exploration Repository (CIDER) was used to search for patients admitted to the Barnes-Jewish hospital inpatient neurology service with the diagnosis of "headache" or "migraine." Patients were then identified as status migrainosus if they met the International Headache Society of a debilitating migraine lasting > 72 hours. Clinical records (History & Physicals, Discharge Summaries, medication administration record and pain scales) were then entered into a secure online database (REDCap).

Results: Forty-three patients with the diagnosis of migraine between 2008 and 2015 received 10 to 40 mg of oral or intramuscular ziprasidone for the treatment of status migrainosus. Among patients that received ziprasidone, headache severity decreased from 8.97 $\pm$ 0.24 on admission to 3.26 $\pm$ 0.49 ($p<0.00001$) on discharge. Ziprasidone was the definitive medication leading to discharge in 65% of reported cases. The thirty day readmission rate for migraine headache in patients that received ziprasidone was 11%. Ziprasidone was well tolerated with side effects (N=3) limited to upper back stiffness concerning for a dystonic reaction, rhinorrhea and a prolonged QTC of 495.

Conclusions: The findings of this study suggest that ziprasidone may be a safe, effective abortive medication for the treatment of status migrainosus. Future directions include plans for a retrospective case-control study among the Barnes-Jewish Hospital population, comparing ziprasidone to standard of care.



Malbrough, Thomas

Intravascular Large B-cell Lymphoma Presenting as Multifocal and Recurrent Ischemic Strokes: A Case Report

Case Description: 78 year-old female with multifocal, recurrent ischemic strokes over a 10 month period.

Setting: Inpatient Rehabilitation Hospital

Clinical Course: This patient was admitted to the hospital for a decline in cognitive function, balance and mobility. She had a history of 3 prior multifocal ischemic events within the preceding 10 months. Her examination exhibited L>R sided dysmetria, L babinski, and slightly reduced LLE sensation. MRI showed multifocal punctate areas of diffusion restriction and T1 hyperintensity in R parietal and occipital gray matter consistent with infarctions. Cerebral angiogram revealed inappropriate caliber changes of the cerebral and cerebellar arteries suggestive of possible vasculitis. General chemistry, hypercoagulability, and echocardiogram tests were normal. CT scans and CSF evaluation for possible malignancy were negative. Prior to transfer to inpatient rehabilitation she was diagnosed with atrial fibrillation and started on warfarin. Modest improvements were made during rehab and she was discharged home. Shortly thereafter she had another acute decline in her functional and cognitive status, exhibiting left neglect and inattention with markedly decreased balance and mobility. Repeat MRI revealed new punctate areas of multifocal, bilateral acute infarctions despite a therapeutic INR. Neurosurgery subsequently performed a brain biopsy of the cerebellar cortex revealing a diagnosis of IVLBCL. Immunochemotherapy regimen with R-CEOP was initiated a week later while continuing therapy. She was eventually discharged from rehab to a tertiary extended care facility having made significant overall improvements.

Discussion: IVLCBL is characterized by intravascular growth of neoplastic CD20-positive large B cells leading to the formation of small-vessel clots causing ischemic lesions. The hallmark of IVLBCL with cerebral involvement is the triad of subacute encephalopathy, multiple strokes, and elevated serum LDH. Cerebral vasculitis, septic encephalopathy, or infections of the CNS are the commonly considered diagnoses. Brain biopsy is the diagnostic procedure of choice when IVLBCL may be suspected. Conclusions: Intravascular large B-cell lymphoma is a rare and typically fatal cause of recurrent ischemic strokes which requires early invasive testing to provide proper treatment and improve prognosis.

Mitchell, Kyle

Bilateral Subthalamic Nucleus Deep Brain Stimulation in Elderly Patients with Parkinson Disease

Kyle Mitchell, MD, Scott Norris, MD, Samer Tabbal, MD, Joshua Dowling, MD, Keith Rich, MD, Joel Perlmutter, MD, and Mwiza Ushe, MD

OBJECTIVE: To evaluate the efficacy and safety of bilateral subthalamic nucleus deep brain stimulation (STN DBS) for the motor symptoms of idiopathic Parkinson Disease (PD) in patients 75 years and older, and to compare the risks and benefits to a younger cohort.

BACKGROUND: STN DBS is a commonly practiced and effective treatment for moderated to advanced PD. Clinical studies have shown improvement of motor function and quality of life, but often exclude patients older than 75 years.

METHODS: 91 patients (46<75 years old, 45>75 years old) with STN DBS were retrospectively analyzed. The primary outcome measures were changes in unified Parkinson disease rating scale subscale III and IV (UPDRS III and IV) at 6 months and 1 year after surgery compared to presurgical evaluation in an intention to treat model with the last evaluation carried forward. Secondary outcome measures were changes in UPDRS I and II subscales. DBS and surgery related complications and survival were evaluated in both groups.

RESULTS: 23 patients were censored due to inadequate follow up, but were included in the adverse events analysis. In the older cohort, STN DBS improved UPDRS III at 6 months (mean±SD) (38.7%±21.8%, $p<0.001$) and 1 year (36.7%±28.2%, $p<0.001$) as well as UDPRS IV at 6 months (-1.2±1.9 points, 19 improved, 4 worsened, $p<0.001$) and 1 year (-1.3±1.7 points, 19 improved, 3 worsened, $p<0.001$). The older cohort had worsened UPDRS I at 1 year (1.3±2.2, 19 worsened, 5 improved, $p<0.005$) and no change in UPDRS II. There was no difference in primary or secondary outcomes between the younger and older cohorts. Two patients in the younger cohort and five patients in the older cohort died prior to 1 year follow up. Only one patient died as a direct result of DBS surgery. The groups had a similar number of device infections (2/46 and 1/45) and lead malfunctions (1/46 and 2/45). One patient suffered a fatal postoperative intraparenchymal hemorrhage, and one other patient was found to have a small intraventricular hemorrhage, both in the older cohort.

CONCLUSIONS: Bilateral STN DBS provides similar dramatic motor benefit and reduction in dyskinesia in younger and older patients. In our cohort, older patients had a higher incidence of hemorrhage and all-cause mortality at 1 year, though the risk was relatively small. DBS remains effective regardless of age.

Newman, Blake

Rates of ADC and FLAIR signal maturation depend on depth of ischemia and time: Helpful for determining time of onset?

Abstract: Approximately 30% of stroke patients have an unclear onset of stroke symptoms causing ineligibility for IV tPA treatment. An MRI biomarker, "Diffusion-FLAIR mismatch", has shown promise as a "clock" to estimate the stroke onset time when it is unknown. In addition to time, the severity of ischemia likely influences the rate of FLAIR and diffusion signal evolution. In a cohort of patients with witnessed stroke onset, we studied FLAIR and apparent diffusion coefficient (ADC) signal maturation on sequential MRIs as a function of severity of ischemia to understand how the severity of ischemia may influence the rate of signal change beyond time alone. A general linear model was created evaluating ADC, FLAIR, and mean transit time (MTT) for prediction of stroke onset time. Rates of FLAIR and ADC change and FLAIR positivity were influenced by time from stroke onset and severity of ischemia. While FLAIR demonstrated perfusion-dependent change beyond 6 hrs, ADC matured at 6 hrs, showing little change beyond. nFLAIR and pMTT at moderate ischemic severity (pMTT ≥ 10 or 12s) were predictive of stroke onset time with excellent sensitivity and specificity for determining IV tPA eligibility within 4.5 hours. Understanding factors which influence MR signal change may help refine an imaging biomarker for determining the time of stroke onset.

Ong, Charlene

Endovascular Thrombectomy for Anterior Circulation Stroke: A Systematic Review and Meta-analysis

***Charlene J. Ong MD, *Chester K. Yarbrough MD, Alexander B. Beyer BS, Kim Lipsey MLS, Colin P. Derdeyn MD**

Object: Stroke affects approximately 700,000 patients annually, and causes significant morbidity and mortality. Efforts to decrease associated morbidity have led to advances in thrombolytic therapy, including the development of mechanical devices that remove large intra-arterial thrombi, referred to as endovascular thrombectomy (ET). Several recent randomized controlled trials (RCTs) comparing ET to intravenous t-PA (IV-tPA) have shown effectiveness of ET for a subset of stroke patients. The study objective is to pool odds ratios of multiple RCTs and high-quality cohort and case series to evaluate the effect of ET on good outcome in stroke patients.

Methods: We searched PubMed, Embase, Web of Science, SCOPUS, ClinicalTrials.gov and Cochrane databases to identify original research publications between 1996 and 2015 that: a) reported clinical outcomes in patients for stroke at 90 days with the modified Rankin Score (mRS); b) included at least 10 patients per group; c) compared outcome to a control arm and d) included more than 90% of anterior circulation strokes in each arm. Two authors reviewed manuscripts for inclusion independently. Effect estimates were analyzed using a random effects model.

Results: Seventeen of 23,809 studies met inclusion criteria. ET was associated with increased odds for good outcome (OR 1.69 [1.35, 2.12]). In subgroup analysis, younger patients had increased odds of good outcome, (OR 1.66 [1.27, 2.16], and in older subgroups, odds of mRS 0-2 at 90 days was just shy of significance (OR 1.53 [0.99, 2.36]). Studies showed an increased odds for good outcome with ET regardless of whether patients received IV-tPA prior to intervention or not (OR 1.72 [1.40, 2.10]; OR 1.63 [1.10,2.42]). ET was also shown to be superior in both subgroups of patients with severe and moderate strokes (OR 1.99, [1.52,2.62]; (OR 1.56 [1.13,2.16]). No evidence of publication bias was seen. Symptomatic intracranial hemorrhage (OR 1.25 [0.86,1.83]) and mortality (OR 0.85 [0.71,1.03]) was similar between ET and control patients. Recent RCTs suggest a NNT of 5 for confirmed large vessel occlusion causing anterior circulation stroke.

Conclusions: ET improves good outcomes after anterior circulation stroke. Symptomatic intracranial hemorrhage risk and mortality is similar between ET and control. Based on these results, ET should be strongly considered for all patients with a stroke affecting a proximal vessel of the anterior circulation without a contraindication to ET.

Patchala, Sri

Predictors of Acute Care Transfers in Patients with Brain Tumor Admitted to Inpatient Rehabilitation

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1Division of Neurorehabilitation and Department of Neurology, Washington University School of Medicine (WUSM); 2Department of Quality Improvement, The Rehabilitation Institute of St. Louis (TRISL) 3Department of Medicine, WUSM

Background: Acute care transfers (ACT's) are common in inpatient rehabilitation settings; especially in facilities affiliated with tertiary care referral hospitals that serve patients with many co-morbidities. Tools are needed to identify patients most appropriate for successful inpatient rehabilitation stays.

Objective: We created a subcommittee, the Falls and Acute Care Transfer (FACT) Committee within our Quality Improvement process that was directed to review our ACT rate and identify risk factors for transfer back to the hospital in patients with diagnoses of primary or secondary brain tumor.

Methods: We had completed a chart review of 175 TRISL patients in 2012 with a primary admitting diagnosis of non-traumatic brain injury (NTBI), a group at elevated risk for ACTs. We identified another 95 TRISL patients with NTBI in 2014. Using these two data sets, we identified 74 patients with a diagnosis of primary or secondary brain tumor. We reviewed the patient records for ACT risk factors.

Results: Braden pressure sore risk scores, lower 02 sat rates and lower functional status on admission were associated with higher rates of ACTs. Basic FIM® scores (0-28) were fair predictors based on ROC/AUC (.71). Using a cut-off score of 16 resulted in best discrimination for d/c home.

Conclusions: We have created a process to identify risk factors for ACTs that should aid clinicians when admitting patients and provide a safety net to those patients who are at high risk for ACTs. Categorization of samples into high risk medical diagnoses will likely improve model prediction. Further study in larger sample sizes is needed to validate our findings and develop predictive models of acute care transfer risk.

Patel, Kevin

Early Diffusion Evidence of Retrograde Trans-synaptic Degeneration in the Human Visual System

Objective: Retrograde trans-synaptic degeneration (RTD) of the visual system is associated with measures of visual impairment though its contribution is unclear. Noninvasive measures of have not been shown to be sensitive to RTD in the period during which visual recovery occurs. We investigated whether DTI markers of white matter health would offer sensitive and early markers of RTD.

Methods: We performed a prospective longitudinal analysis of the sensitivity of diffusion tensor imaging (DTI) markers of microstructural integrity of the optic tract in twelve patients with stroke to the postgeniculate visual system, twelve stroke control subjects, and twenty eight healthy controls. We examined group differences in 1) optic tract (OT) fractional anisotropy asymmetries (FA-Asymmetry), 2) perimetric measures of visual impairment, and 3) the relationship between FA-Asymmetry and perimetric assessment.

Results: FA-Asymmetry was higher in patients with post-geniculate lesions than in patients with stroke elsewhere and in healthy controls. These differences were evident three months from the time of injury and did not change significantly at twelve months. Perimetric measures showed evidence of impairment in subjects with visual pathway stroke but not in control groups. A significant association was observed between FA-Asymmetry and perimetric measures at three months which persisted at twelve months.

Interpretation: DTI markers of RTD are evident three months from the time of injury. This represents the earliest noninvasive evidence of this change in any species. Further these measures associate with measures of behavioral impairment. DTI measures offer an easily reproducible, non-invasive and sensitive method of investigating RTD and its role in visual impairment.

Riordan, Heather

MRI Findings in a Child with Acute Hepatic Encephalopathy Mimicking Hypoxic-ischemic Encephalopathy

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OBJECTIVE: To describe the MRI abnormalities mimicking hypoxic ischemic encephalopathy (HIE) and clinical outcome in a child after liver transplant for acute hepatic encephalopathy.

METHODS: Case report.

RESULTS: A 3-year-old boy presented to St. Louis Children's Hospital in idiopathic hepatic failure. Ammonia peaked at 207 mcmol/L on day 6, accompanied by severe encephalopathy, but intact cranial nerves and a normal head CT. He underwent liver transplant on day 7. The following day, his neurologic status worsened, with loss of gag reflex. CT revealed diffuse gray-white hypoattenuation. MRI on day 10 showed diffuse diffusion restriction in a non-vascular pattern (Figure 1). His exam gradually improved over his 2-month hospitalization. MRI on day 27 showed improvement in diffusion restriction and increased T2/FLAIR changes (Figure 2). At 3-month follow-up, he speaks in 4-5 word sentences, follows commands, feeds himself, and walks independently.

CONCLUSION: Diffusion-restriction associated with hepatic encephalopathy can be confused with HIE. Our patient demonstrates that this process can occur in the subacute period after the liver failure is corrected. The mechanism may be due to accumulation of glutamine in astrocytes causing increased intracellular osmotic pressures and cerebral edema, which is not quickly reversed.1 This cascade may explain our patient's presentation of decompensation post-liver transplant. Reports of adults with hepatic encephalopathy have also found reversible cortical diffusion restriction radiographically indistinguishable from HIE.2,3,4,5 Our patient's outcome was better than expected for HIE. Awareness of this phenomenon aids prognostication and directing goals of care.

KEY WORDS: Encephalopathy, Hepatic Failure, Hyperammonemia, MRI

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Riordan, Heather (continued)

FIGURES:

Figure 1: Diffusion weighted and FLAIR sequences from MRI on day 10 of hospitalization, demonstrating diffuse diffusion restriction throughout the peri- ventricular, cortical and subcortical white matter with hyperintensity of the deep-grey structures.

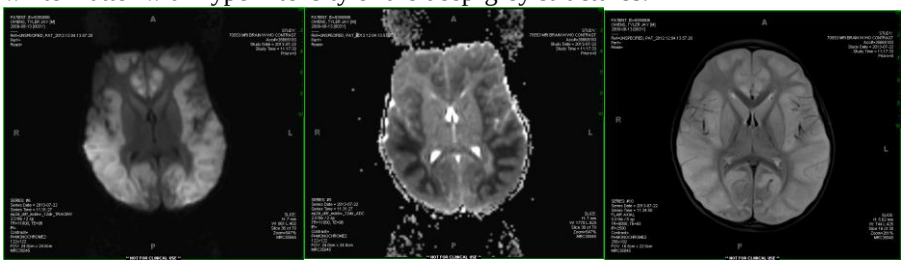
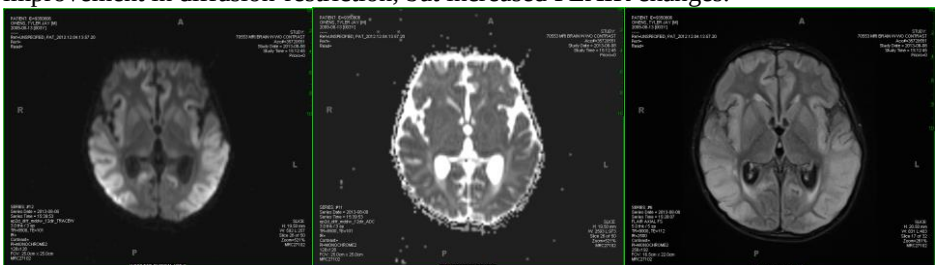


Figure 2: Diffusion-weighted and FLAIR sequences from MRI on hospital day 27 showed improvement in diffusion-restriction, but increased FLAIR changes.



Schulte, Adam J.

Neuromyelitis Optica during Pregnancy in an Adolescent Patient

Adam J. Schulte, MD and Rimma Ruvinskaya, MD

Abstract: Neuromyelitis optica (NMO) is an uncommon, usually idiopathic, segmental spinal cord injury caused by inflammation. There are several case reports of onset of NMO during pregnancy, but none in the pediatric population. We report the case of a 15-year-old patient, pregnant at 12 weeks' gestation, who presented with low back pain and rapidly progressive weakness and leg paresthesias. Magnetic resonance imaging and cerebrospinal fluid were diagnostic of NMO. The pregnancy was electively terminated and she was treated with plasmapheresis, corticosteroids, rituximab, and mycophenolate mofetil (MMF). She remains paraplegic but without further relapse while maintained on MMF.

Soleimani-Meigooni, David

JC Virus Granule Cell Neuronopathy in the Setting of Chronic Lymphopenia Treated with Recombinant Interleukin-7

Abstract: JC virus (JCV) is a polyomavirus associated with several phenotypes of central nervous system infection in immunocompromised patients, including progressive multifocal leukoencephalopathy. A less common phenotype, known as JCV granule cell neuronopathy (JCV-GCN), occurs when the virus predominantly infects cerebellar granule cells, resulting in ataxia. This tropism has been associated with mutations in the VP1 capsid protein of JCV. We report a case of JCV-GCN in a 77-year-old man with two months of subacute progressive ataxia, rendering him non-ambulatory at the time of presentation, and an inflammatory cerebrospinal fluid (CSF) profile (protein 58 mg/dL, glucose 86 mg/dL, nucleated cells 52/µL [88% lymphocytes], quantitative JCV PCR 1328 copies/mL) in the setting of chronic lymphopenia (absolute lymphocyte count, 300-700/µL) following chemotherapy for mantle cell lymphoma. CSF cytology, flow cytometry, oligoclonal bands, and cerebellar and paraneoplastic antibodies were negative. A thorough screen for other etiologies of cerebellar ataxia was unrevealing. MRI imaging could not be obtained because of an incompatible pacemaker. Cerebellar biopsy demonstrated histopathology consistent with JCV-GCN. Preliminary nucleotide sequencing of the VP1 capsid-encoding region of JCV recovered from biopsy tissue did not show any known JCV-GCN mutations. His ataxia improved with intravenous immunoglobulin, high-dose intravenous methylprednisolone, and mirtazapine and mefloquine, as did his CSF profile despite an increase in his CSF JCV viral load (protein 67 mg/dL, glucose 86 mg/dL, nucleated cells 4/µL, quantitative JCV PCR 2394 copies/mL). IL-7 therapy was administered (20 µg/kg subcutaneous injection) once a week, for a total of three weeks. His ataxia improved to the point of ambulating a few steps without falling. A lumbar puncture performed after completion of IL-7 therapy showed a protein of 71 mg/dL, glucose 55 mg/dL, nucleated cells 49/µL [73% lymphocytes], and quantitative JCV PCR 37 copies/mL. One month after his last dose of IL-7, he presented with worsening ataxia. His peripheral lymphocyte count had increased to 1500/□L and his lumbar puncture showed protein 78 mg/dL, glucose 55 mg/dL, and nucleated cells 49/µL [93% lymphocytes]. Given the differential diagnosis of immune reconstitution inflammatory syndrome as a cause of his recurrent ataxia, he received treatments of high-dose intravenous methylprednisolone and he was also restarted on mirtazapine and mefloquine. Unfortunately, he continues to decline. He cannot walk and he struggles to sit upright without support. His most recent lumbar puncture, performed in the setting of weekly 1 gram methylprednisolone infusions, showed a protein of 52 mg/dL, glucose 65 mg/dL, nucleated cells 21/µL [93% lymphocytes], and quantitative JCV PCR 65 copies/mL.

Yuan, Qingyang (Kristy)

CSF Volumetric Analysis Reliably Quantifies Cerebral Edema and Correlates with Clinical Deterioration in Large Hemispheric Infarcts

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Background: Malignant cerebral edema complicates at least 20% of large hemispheric infarcts (LHI) and carries high risk of mortality. Edema results from the complex interplay of multiple cellular pathways. Genetic analysis of edema may provide insights into its pathogenesis and novel targets for prevention but requires an accurate quantitative metric. Midline shift (MLS) is a standard but crude measure of edema severity. Progressive reduction in CSF compartments may better capture the spectrum of edema. We propose that volumetric analysis of CSF compartments provides a reliable and valid means of quantifying the severity and kinetics of edema after LHI.

Methods: We retrospectively identified patients enrolled in a study of genetic contributors to stroke recovery from 2008-2013. Inclusion criteria: baseline NIHSS ≥ 8 and baseline CT < 6 hours after stroke onset; at least 1 follow-up CT at "peak edema" (2-5 days after onset); a subset also had earlier CT at 4-48 hours after stroke for the study of edema kinetics over serial CTs. Excluded: those with parenchymal hematoma on any CT. Using NIH MIPAV software, the volumes of sulci and lateral ventricles ipsilateral (IL) and contralateral (CL) to the infarct on baseline and serial CTs were quantified by two raters, as was peak infarct volume and MLS. Inter-rater reliability of the volumetric method was evaluated by intra-class correlation coefficient. Change in compartment volumes from baseline to peak edema was correlated with peak edema MLS and clinically significant "malignant edema," defined as MLS ≥ 5mm requiring hemicraniectomy, osmotic therapy, or associated with decline in GCS.

Results: Seventeen patients were analyzed (median NIHSS 16, IQR 12-21; time to peak edema CT 79 hrs, IQR 64-102). Inter-rater reliability for volume measures was excellent (intraclass correlation >0.97). Total CSF volume dropped by 43% at peak edema. Greatest reductions were in IL sulci and IL ventricular volumes (79%, 61%, respectively). The steepest decline in CSF volumes occurred within 48 hrs. of baseline CT, whereas MLS sharply rises after 48 hrs. when CSF compensation is exhausted. Peak edema infarct volume correlated with MLS (r=0.74, p=0.001), as did total change in CSF volume, and % reduction in CL sulci volume, which remained significant (r=0.76, p=0.001) even after correcting for infarct volume. Infarct volume significantly correlated with malignant edema (median 306ml vs. 139ml, p=0.04), but as did total change in CSF volume (median -69 ml vs. -37ml) and % reduction in CL sulci volume (median -53% vs. -23%).

Conclusions: CSF volumetrics is a reliable tool for quantifying cerebral edema and a novel method for studying edema kinetics, with the majority of CSF shifts occurring within 48 hrs of LHI. These metrics may be ideally suited to future larger-scale study of genetic markers of edema development after LHI. Total CSF reduction from baseline and percentage reduction in CL sulcal volume correlate best with MLS, independent of infarct size. These volume changes have a broader dynamic range and thus may be better indicators of edema severity than MLS. The CSF metrics also distinguish those with malignant edema from those with a more benign course, further validating their utility.

Zhang, Lynn

Central Nervous System Tuberculosis Presenting as Encephalopathy

Abstract: Mycobacterium tuberculosis (TB) infection is a worldwide epidemic that annually infects about 9 million people and kills about 1.5 million. Central nervous system (CNS) TB affects about 1% of TB patients and can have nonspecific manifestations which can cause substantial morbidity and mortality if unrecognized. It most commonly causes tuberculous meningitis and presents with typical signs of headache, fevers and nuchal rigidity. Less commonly, it can cause cranial nerve palsies, encephalitis, hydrocephalus and other focal signs from mass effect. Early recognition and treatment with RIPE and adjunctive steroids is critical as morbidity is directly linked to early treatment.