Washington University
School of Medicine
Department of Neurology

Residents' Day Symposium
Friday, June 3, 2016
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.

Ahuja, Michael

Early Recognition & Management of Post Stroke Pain In Acute Inpatient Rehab

Michael Ahuja MD, Prateek Grover MD, and David Carr MD

Abstract: Pain affects almost 50% of people with stroke in the acute phase setting (e.g. inpatient rehabilitation), and impacts quality of life and function negatively. Challenges to addressing this high frequency of pain in the inpatient setting include inadequate daily pain tracking-mechanisms and inability to maximize function due to missed therapy. The former has been observed to be associated with the latter at our inpatient facility. Accordingly, a clinical tool to accurately track both daily pain scores and missed therapy units (MTUs) during inpatient stroke rehabilitation could allow early recognition and intervention, and ultimately maximize functional gains and discharge outcomes.

This QI project included three phases 1) evaluating the association between post-stroke pain, MTUs, and functional gains 2) designing a pain and MTUs tracking clinical tool, and 3) evaluating the impact of this tool on functional gains. For phase one, a retrospective chart review of the acute inpatient stroke service at The Rehabilitation Institute of St. Louis, MO, from January-July 2014 (n=94) was conducted. Data collection focused on demographics, stroke pathology, average maximum pain scores (avgMaxPain), tMTUs, and Functional Independence Measure (FIM) gains. Data analysis included avgMaxPain and tMTU stratification, evaluation of their strength of association, and their independent relationship with FIM gains. We are currently at phase two, refining the clinical tool to collect pain and MTU data prospectively.

The avgMaxPain score showed a fair correlation with tMTUs (corel coefficient=0.57), with a stronger relationship for length of stay exceeding 15 days (0.622). Also, as expected, tMTUs were inversely correlated with FIM gains (-0.28). Based upon this relationship, we proposed 1) integrating pain as the 6th vital sign on the EMR physician dashboard, with severity-based red-flagging, and centralized team member (nursing, therapy, physician) reporting. 2) obtaining MTUs from therapy daily. After many months of review, the EMR team was unable to implement this change due to incompatibility of reporting systems assigned to team members.

Having learnt that design does not equal execution, we have modified our intervention to a paper-based form documenting both pain and missed therapy units daily. This tool is aimed to emphasize daily recognition and enhance interdisciplinary discussion of pain score trends. The form has support for implementation starting January 2016 from nursing, therapy, risk management, and resident physicians, highlighting teamwork integral to a QI project. We hope to show that our intervention tool improves pain management, reduces MTUs, and improves functional outcomes in our inpatient stroke population.

Albertson, Asher

Is Axonal Sprouting required for Cortical Remapping after Ischemic Brain Injury?

Albertson AJ, Kraft A, Yang X, Xiao Q, and Lee JM

Abstract: Spontaneous recovery after stroke, the most common cause of adult disability worldwide, is unpredictable and often incomplete. In cases of infarction involving the cortex, several studies suggest that functional representations intrinsic to infarcted tissue "remap" to perilesional cortex. This remapping is associated with behavioral recovery. Moreover, whole-brain functional connectivity, which is acutely disrupted after stroke, is also restored in patients who recover. It has been postulated that axonal sprouting plays a role in behavioral recovery, but the molecular mechanisms and specific neuronal circuits involved in remapping are not defined. One candidate gene mediating post-ischemic axonal sprouting is Growth Associated Protein 43 (GAP43). Expressed in growth cones of sprouting axons and necessary for both extension and targeting, GAP43 is essential for the formation of neuronal connections during development. In the adult brain GAP43 is expressed at low levels, but it is strongly upregulated following ischemic injury, suggesting a role in post-injury repair. We have developed an AAV vector carrying GAP43 shRNA and GFP, which significantly reduces GAP43 expression in cultured neurons and induces widespread GFP expression within thalamic neurons and their cortical projections. Using viral gene transfer, we propose to silence GAP43 in thalamic, perilesional, or contralesional neurons following focal ischemia (photothrombosis) to the forepaw somatosensory cortex. This ischemic injury shows remapping and recovery in the weeks following infarction. We will determine if axonal sprouting from these distinct regions is necessary for somatosensory remapping and behavioral recovery. In addition, we will use functional connectivity optical intrinsic signal imaging (fcOIS) to determine if axonal sprouting-dependent remapping is required for recovery of functional connectivity throughout the brain.

Baldassari, Laura

Modified EDSS for Use in Multiple Sclerosis Clinical Practice

Laura E Baldassari, MD, MHS1, Amber Salter, PhD2, Erin E Longbrake, MD, PhD1, Anne H Cross, MD1 and Robert T Naismith, MD1

(1)Neurology, Washington University School of Medicine, St Louis, MO, (2)Biostatistics, Washington University in St. Louis, St. Louis, MO

Background: The Expanded Disability Status Scale (EDSS) is the standard research measure of disability in multiple sclerosis (MS). Limitations for clinical use include time required for administration, scoring complexity, and technique redundancy. If simplified, the EDSS would provide a standardized numerical rating to monitor disease progression and treatment response in the clinical setting.

Objectives: To develop a modified version of the EDSS (mEDSS) for clinical monitoring and compare this modified version to the full EDSS.

Methods: The existing EDSS was modified in several ways, via consensus among 3 MS specialists, to create the mEDSS: exam maneuvers which do not impact function were eliminated (e.g. reflexes), redundant maneuvers were consolidated (e.g. proprioception), and scoring of functional systems was simplified. The mEDSS was designed to reflect a more concise EDSS that utilizes exam techniques important for clinical monitoring. Existing data from the CombiRx trial was used to ensure standardized ascertainment of the EDSS; from these data, we derived the mEDSS. The mEDSS and EDSS, as well as each functional system (FS), were compared using Spearman's rank correlation coefficients and Bland-Altman plots. Discrepancies within each FS between the EDSS and mEDSS were delineated within a subset with physical charts available for review.

Results: The mEDSS at the baseline CombiRx trial visit (n=1005) was derived and EDSS values ranged between 0 and 6. The mEDSS had strong correlation with the EDSS, both overall (Spearman's rho = 0.88, $p<0.0001$) and for each functional system (Spearman's rho between 0.64 and 0.97, p-values<0.001). Bland-Altman plots to examine agreement will be presented. The algorithm to derive mEDSS from the EDSS information was validated and discrepancies in functional systems were identified in the chart review. Reasons for discordant scores will be delineated.

Conclusions: The mEDSS was strongly correlated with the full EDSS and can therefore provide a useful measure of disability in clinical practice. The development and validation of an automated statistical algorithm enabled us to compare the mEDSS and EDSS in a large population to examine differences in scoring. Longitudinal assessment of the mEDSS for stability and relapse sensitivity is in progress. Future work will examine the practicality and interrater reliability of the mEDSS.

Choi, Justin

Rehab of Non-vasculitic Autoimmune Inflammatory Meningoencephalitis: A Case Report

Case description: 65M with progressive ataxia and dementia

Clinical Course: A previously healthy patient developed progressive ataxia for a year before developing a cognitive decline for three months. After a fall, he was hospitalized for left frontal and left posterior parafalcine subdural hematomas, along with facial fractures. He was admitted to rehabilitation for encephalopathy until he could tolerate further workup. After an extensive workup including EMG and brain biopsy, the patient was diagnosed with Nonvasculitic autoimmune meningioencephalitis (NAIM).

He returned to rehabilitation, and his second hospitalization was punctuated by fluctuant periods of functional gains relative to pulsed steroid infusions. At his worst, he could not sit unsupported, feed himself, and was minimally verbal. After infusions, he was able to transfer with minimal assistance, ambulate with a wheeled walker, feed himself, and speak in simple sentences. Collaboration between the rehabilitation team and the neurology team guided immunomodulatory treatment and a transition to high dose oral steroids. This made it possible to advance the patient's functional progress despite his devastating pathology.

Eight months later, he is a household ambulator and has increasing awareness of his deficits.

Discussion: NAIM's progressive presentation can mimic such clinical entities as Creutzfeldt-Jakob Disease, Hashimoto's encephalopathy, and Sjogren's encephalopathy. Its treatable and reversible nature makes diagnosis especially important in the rehabilitation setting should patients arrive with otherwise inconclusive etiologies.

Conclusion: Nonvasculitic autoimmune meningioencephalitis is a rare clinical entity. A Pubmed query for this diagnosis yields seven results. It remains a diagnosis of exclusion, presenting as progressive ataxia and dementia that is responsive to immunomodulatory agents. If diagnosed early, symptoms can be reversible. If diagnosed late, as in this case, symptoms can plateau at a relatively low functional level. Early diagnosis of NAIM can facilitate efficient use of healthcare resources in rehabilitation as well as improve clinical outcomes.

Creighton, Andrew

Use of Diagnostic Ultrasound for an Atypical Presentation of Low Back Pain in a Young Adult Male: A Case Report

Andrew Creighton DO, Charles Andrus MD, and Chi-Tsai Tang

Disclosure: None

Setting: Tertiary University Orthopaedic Department

Patient: 34 year-old male, with right-sided low back pain (LBP) 32 months following right inguinal hernia repair.

Case Description: The patient reported onset of LBP 22 months after right inguinal hernia repair when he fell down stairs with concurrent trauma of a sledgehammer hitting his lumbar region. Prior treatment included: physical therapy (PT), injections (sacroiliac joint, L4 epidural steroid injection, right L5-S1 medial branch blocks, right superior cluneal nerve block, trigger point injections) and acupuncture. After minimal relief, he presented to the physiatrist for further evaluation. On examination, palpation over the right inguinal hernia scar reproduced the patient's pain in the right lumbar spine region. Diagnostic ultrasound using high frequency 15-4 Mhz probe revealed a hypoechoic, localized area of tissue that connected with and distorted the shape of the ilioinguinal nerve. This area was injected under ultrasound guidance with 1cc of 1% lidocaine and 1cc of 0.25% bupivacaine. Immediately after the injection the patient noted 25% relief of his LBP, increasing to 50% relief after 12 hours. The working diagnosis was referred pain to the right low back related to an entrapped ilioinguinal nerve. The patient was referred to his general surgeon who completed a resection of the ilioinguinal nerve under local anesthesia and ultrasound guidance, enabling the surgeon to direct the intervention to the specific area that reproduced the patient's pain.

Assessment/Results: Two month post-operative follow-up revealed 50% improvement of the patient's LBP and improved function. With less pain inhibition, the patient is participating in PT to reactivate his core and stabilize his lumbopelvic region.

Discussion: Prior cases of pain associated with ilioinguinal nerve injury have focused on a groin pain presentation. The patient in this case complained of right LBP.

Conclusion: Ilioinguinal nerve entrapment can be an unusual source of LBP.

Decker, Gregory

Persistent Hiccups after an Epidural Steroid Injection Successfully Treated with Baclofen: A Case Report

Abstract: A 69 year-old male with a 5-week history of low back pain and left leg pain in the posterior thigh and calf presented for a left S1 transforaminal epidural steroid injection. The day following the injection, he developed hiccups that persisted for 5 days despite non-pharmacologic/conventional treatments. The patient was prescribed baclofen 10 mg PO every 8 hours as needed, and was instructed to contact the clinic the following day with an update. The patient reported complete resolution of his persistent hiccups after two doses of the baclofen. He reported 75% pain relief two weeks after the injection, but eventually pain returned. He had a repeat left S1 transforaminal epidural steroid injection six weeks after the initial injection, and again developed hiccups the following day. He repeated the oral baclofen and the hiccups resolved within two doses once again. Persistent hiccups are an established adverse reaction to epidural steroid injections. This is first case report, to our knowledge, that demonstrates oral baclofen to be effective in treating persistent hiccups following epidural steroid injections.

Dietz, Alexander

Nerve ultrasound identifies abnormalities in the posterior interosseous nerve in patients with proximal radial neuropathies

Abstract: Injuries to the radial nerve and its distal motor branch, the posterior interosseous nerve (PIN) are common and can occur at multiple sites. Clinical exam and electrodiagnostics (EDX) may not be able to identify multiple lesions along the nerve. Nerve ultrasound (NUS) can visualize multiple lesions along the course of a single nerve and might augment EDX.

Findlay, Andrew

Novel Homozygous Recessive MYH2 Variant Associated With An Autosomal Dominant Clinicopatholoical Phenotype

Abstract: Mutations in MYH2 cause both dominant and recessively inherited myopathies. Patients with dominantly inherited MYH2 missense mutations present with congenital joint contractures that resolve with age, external opthalmoplegia, and later onset progressive proximal limb weakness. Muscle biopsy reveals rimmed vacuoles and intranuclear and cytoplasmic inclusions, prompting this entity to initially be described as hereditary inclusion body myopathy 3. In contrast, a distinct phenotype occurs in patients with recessive MYH2 mutations. These patients also have severe opthalmoplegia but instead have a more mild and diffuse pattern of weakness that is early in onset and largely non-progressive. Muscle biopsy reveals small or absent type 2a fibers with no vacuole or inclusion pathology. We identified a patient with childhood onset opthalmoplegia, progressive proximal muscle weakness beginning in adolescence, and muscle biopsy with myopathic changes and rimmed vacuoles. Although this patient's disease course and histopathology is consistent with patients carrying dominant MYH2 mutations, whole exome sequencing revealed a novel c.737 G>A p.(Arg246Thr) homozygous MYH2 variant. These findings expand the clinical and pathologic phenotype of recessive MYH2 myopathies.

Giles, James

The impact of hospital patient-sharing networks on inpatient mortality

Giles JA, Dhand A, Luke DA, and Olsen MA

Abstract:

Introduction: Standardized mortality ratios are statistical tools that compare a hospital's observed death rate with that expected based on patient admission characteristics. Such an approach to mortality modelling does not acknowledge the role of contextual factors related to the characteristics of individual hospitals. One such characteristic includes a hospital's position a structural networks that arises via shared patients. We aimed to determine the role of hospital contextual factors, including network factors, in the prediction of inpatient mortality.

Method: We used administrative data from the Healthcare Cost and Utilization Project's (HCUP) 2011 California State Inpatient Database (CA SID) and State Emergency Department Database (CA SEDD). Using admission data, we constructed patient-sharing networks for all hospitals listed in both the SID and SEDD. Using patient and hospital data (including network statistics), we developed two-level hierarchical models of mortality. Based on this modelling, we determined the contribution of network characteristics to inpatient mortality, and analyzed the role of hospital contextual factors on mortality modelling.

Results: 2,550,951 patient visits were included in analysis, with an overall mortality rate of 2.85%. We built a model using only patient characteristics to predict mortality. This was compared to a second model which included in the regression hospital and network factors, in addition to patient characteristics. In terms of network factors, we found that a hospital's degree centrality was associated with reduced mortality. Further, the regression that included contextual hospital and network factors predicted mortality more closely that the traditional model using compositional patient characteristics alone.

Conclusions: Inpatient mortality modelling is improved with the inclusion of hospital contextual characteristics, when compared with the use of patient-level data alone. This effect is most marked with hospital network factors that account for patient movement between institutions. A central position of a hospital within a patient-sharing network is associated with reduced inpatient mortality. This could be due to many reasons and more research is needed to evaluate underlying mechanisms, which may include differing resources, differences in approaches to end-of-life care and the movement of patients closer to home to die.

Grabe, Jonathan

Bilateral head of caudate infarcts: Case presentation of a rare stroke syndrome caused by an uncommon variant in Circle of Willis anatomy.

Abstract:

Introduction: Bilateral basal ganglia infarcts as explained by a single, focal pathologic event are not routinely encountered given their blood supplies come from discrete vascular territories despite the relative proximity of the basal ganglia structures themselves. In fact, given alterations in flow dynamics in and around the Circle of Willis at the time of an infarct, the infracting side may often acquire some collateral flow from the other to limit an area of unilateral infarction. However, when congenital or acquired anomalies in the normal vascular anatomy exist, more commonly encountered pathology can result in an unexpected clinical presentation.

Case Presentation: A 51-year-old female presents with a first episode of acute onset encephalopathy characterized by psychosis, akinetic mutism, utilization behavior, and gait apraxia. She was initially thought to be suffering from carbon monoxide or other poisoning versus Wernicke's encephalopathy. After further investigation, including vascular studies, she was diagnosed with subacute bilateral caudate head, medial frontorbital and hypothalamic infarcts resulting from a internal carotid artery thrombus that had embolized to the ipsilateral anterior cerebral artery with absent contralateral anterior circulation vasculature.

Conclusion: It is important to be able to recognize the constellation of symptoms and mechanism of occurrence of stroke syndromes that do not respect traditional vascular territories due to pre-existing alterations in normal vascular anatomy.

Helis, Jason

Rates of Detection and Clinical Predictors of Infectious and Autoimmune Encephalitis

Helis JA, Fay AJ, Day GS, Bledsoe S, Brown SM, Storch GA and Mar S

Objective: Determine the rates of detection and clinical features of pediatric patients diagnosed with infectious and autoimmune encephalitis at a large pediatric tertiary care center and define clinical features of various viral pathogens and autoimmune-mediated encephalitis.

Background: Viral encephalitis remains a significant cause of neurological dysfunction and disability among children. The incidence of morbidity can be as high as 50% with some pathogens. The clinical features that distinguish patients with various forms of infectious encephalitis are poorly defined, but are relevant for selection of patients for diagnostic testing and treatment. Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis can be more common in children than some forms of viral encephalitis and have similar clinical features.

Design/Methods: Retrospective chart review was done on patients who underwent CSF analysis for viral pathogens and NMDA encephalitis at a large pediatric medical center during 2013 and 2014. The clinical findings of patients with confirmed infectious and NMDA receptor encephalitis were examined and compared between cohorts.

Results: Enterovirus was sent in CSF of 603 patients and confirmed in 58 (9.6%), Parechovirus was sent in 419 patients and confirmed in 31 (7.3%), HHV6 was sent in 75 patients and confirmed in 4 patients (5.4%), HSV was sent in 616 and confirmed in 5 patients (0.8%). Parechovirus cases were more frequently associated with hyperkalemia and/or hypernatremia ($p=0.04$) and increased CSF monocytes ($p=0.005$). Autoantibody testing for NMDA-receptor encephalitis was performed in 53 children, and was positive in two patients (3.7%). Both patients had encephalopathy, abnormal neurological signs, seizures along with psychiatric symptoms

Conclusions: Infectious etiologies of suspected viral encephalitis were confirmed in a minority of patients. The low identification rates may reflect low pre-test probability or limitations in testing. While clinical symptoms were similar in enterovirus and parechovirus cases, parechovirus cases were distinguished by a greater frequency of increased % CSF monocytes and hyperkalemia and/or hyponatremia. Testing for NMDA receptor encephalitis had a low rate of detection in patients without encephalopathy and neurological symptoms. Prospective studies are required to further define clinical features of viral and autoimmune encephalitis to improve selection of those tested for these diseases.

Hepner, Seth

Voltage-gated Calcium Channel Antibodies with Associated Encephalopathy: A Case Series and the Spectrum of Disease

Abstract: Encephalopathy associated with auto-antibodies to voltage-gated calcium channels is a rare entity with only few case-reports in the literature. We describe a case series of five consecutive patients who were evaluated for an encephalopathic process and found to have auto-antibodies to voltage-gated calcium channels, their work-up, clinical courses and response to treatment with immunomodulator drugs.

Kang, Peter

The Spectrum of Sleep Pathology in Definite Creutzfeldt-Jakob Disease

Abstract:

Objective: To identify the prevalence and type(s) of sleep pathology in Creutzfeldt-Jakob disease (CJD).

Background: Sleep disorders are strongly associated with multiple neurodegenerative diseases and impact quality of life. The relationship between sleep and CJD, a rapidly progressive, fatal neurodegenerative dementia, has not been well characterized.

Design/Methods: We performed a retrospective analysis of sleep signs and symptoms in a cohort of patients with definite CJD (n = 28; 26 sporadic, 2 familial; age range 42-76). Polysomnography (PSG) was performed on 14 patients.

Results: While only 5 of 28 patients carried a premorbid sleep diagnosis, signs/symptoms of sleep dysfunction were present in 25. Eleven reported symptoms of hypersomnia, and 13 of insomnia. Seven met criteria for restless legs symptoms and/or periodic limb movements in sleep, and nine reported parasomnias. Of the 14 patients with PSG: One did not show sleep, seven (54%) had poorly formed sleep spindles and/or K-complexes, and ten (77%) met clinical criteria for sleep-disordered breathing; three of 8 (38%) had Rapid Eye Movement (REM) sleep without atonia, two of which met clinical criteria for a diagnosis of REM behavior disorder. Median total sleep time was 226 (IQR = 195-282) minutes. Median sleep efficiency was 58.5 % (IQR = 41 - 65.5 %). Median time in REM sleep was 0.35% (IQR = 0 – 7.125 %). Median periodic limb movement index was 0 per hour (IQR = 0 – 19.825) with 5 patients (42%) demonstrating periodic limb movements on PSG.

Conclusions: Sleep abnormalities are common in CJD and represent a potentially treatable comorbidity associated with this devastating disease. Screening for sleep pathology may be indicated in the evaluation of patients with suspected CJD. Longitudinal studies are warranted to determine the significance of sleep abnormalities in CJD diagnosis and whether sleep measures can serve as biomarkers of disease progression.

Kim, Young-Min

Pediatric Acute Flaccid Myelitis with Neuropathologic Correlate:
The Washington University Experience

Young-Min Kim, MD1, Soe Mar, MD1, and Robert Schmidt, MD2
1Division of Pediatric and Developmental Neurology, Department of Neurology,
2Division of Neuropathology, Department of Pathology and Immunology
Washington University in St. Louis School of Medicine

Acute flaccid myelitis (AFM) associated with the 2014 enterovirus D68 (EV-D68) outbreak is a disabling disease of unclear pathogenesis. We present our case series with long-term neurologic outcomes as well as an unprecedented neuropathologic correlate, which suggests an immune-mediated component to the overall disease process. Current evidence, however, does not support the use of immunomodulatory therapy. Appropriately timed peripheral nerve transfer surgery may improve recovery. Recovery is generally poor although prognosis for injury outside the lower motor neuron may be more favorable.

Landsness, Eric

Using transgenic neuronal calcium signaling (GCaMP) to monitor whole brain sleep

Landsness EC, Wright P, Bauer A, Culver J, and Lee JM

Introduction: The cellular and molecular mechanisms underlying slow oscillations during anesthesia and sleep remain poorly understood. Towards this end, we have utilized transgenic mice genetically encoded to express calcium indicators in cortical neurons (GCaMP mice) to monitor neuronal activity in living mice. We report the neural correlates of ketamine anesthesia sedation and compare them to wakefulness in mice.

Methods: Transgenic mice selectively expressing a Thy1-GCAMP6 protein in cortical layers II-VI were implanted with chronic, through-bone windows (bi-hemispheric, 11 mm A-P by 9 mm M-L) and EEG screws. Optical intrinsic signal imaging (OIS) was utilized to detect calcium-induced fluorescence using blue light and a CCD camera (20Hz) under waking and ketamine anesthesia with simultaneous EEG collection.

Results: There is a significant increase in the spectra content of the GCAMP signal in the 1-2 Hz range during anesthesia compared to wakefulness that are recapitulated in the simultaneously-acquired EEG signal. With the added spatial resolution of OIS, we report a marked anterior to posterior contiguous propagation of GCAMP6 activity similar to previously described propagation of sleep slow waves in humans.

Conclusions: OIS imaging of GCaMP mice provides high spatial and temporal resolution data enabling us to better understand the cortical slow oscillation. By combining this novel imaging approach in mice with powerful genetic and surgical manipulations, we will be able to study molecular mechanisms underlying sleep-related slow oscillations under neuropathological conditions such as acute or chronic brain injury and develop targeted sleep-related interventions.

Liang, Shannon

Dihydroergotamine treatment for status migrainosus in children—efficacy and tolerability

Shannon N. Liang, M.D. and Soe Mar, M.D.

OBJECTIVE: To evaluate the effectiveness and tolerability of intravenous dihydroergotamine (DHE) in children requiring admission for status migrainosus.

BACKGROUND: There is limited evidence about status migrainosus management in children, and lack of an established treatment protocol. Prior studies have reported a 70-80% response to IV DHE, with medication response after about 5 doses.

METHODS: This is a retrospective chart review of 36 patients and 40 admissions, ages 7-18 years, who failed other first line medications at home and/or the emergency department, and were admitted to the St. Louis Children's Hospital from January 2013 to May 2015, for further management with IV DHE. Data were collected on: duration of presenting migraine; medications used prior to admission; effectiveness of DHE treatment based upon pain scores; dose, duration, and frequency of side effects of DHE; and length of admission.

RESULTS: Median duration of the presenting headache was 14 days. The emergency department trialed IV NSAIDs with antiemetics in 68% and IV valproic acid in 40%. Average length of stay was 4.5 days. Most received a 0.2 mg test dose of DHE, then 0.01 to 0.02 mg/kg/dose every 8 hours if tolerated. Mean number of DHE doses was 3.5. After DHE, there was a statistically significant decrease in pain scores (-2.1 points), 2/3 reported decreased pain, 17% were headache-free, and 60% did not require another IV abortive medication. Five percent stopped DHE after the test dose, 65% experienced side effects, and 25% stopped DHE due to side effects.

CONCLUSIONS: Even if refractory to other IV abortive medications for status migrainosus, DHE can be an effective therapy in children (2/3 respond), but may require several doses. The tolerability of DHE may limit its use, as 2/3 of patients experienced side effects, commonly nausea/emesis despite antiemetic pretreatment, and 1/4 stopped DHE due to side effects.

Malbrough, Thomas

Saphenous Nerve Entrapment Case Series

Case Diagnosis: We describe the clinical symptom complex of eight patients with compressive saphenous neuropathy confirmed by successful saphenous nerve release.

Case Description: In a retrospective chart review we obtained data on 8 patients referred to plastic surgery for saphenous nerve release. Our population of subjects primarily developed onset of pain either following surgery or trauma. They presented with a variable distribution of pain, but predominantly it was focused either over the medial aspect of the knee or along the medial aspect of the leg extending from the distal thigh to the ankle. Three subjects had undergone knee surgeries prior to our evaluation attempting to improve their symptoms. All subjects underwent a saphenous nerve release while some underwent additional nerve decompressions often including the infrapatellar saphenous branch (IPS).

Discussion: The saphenous nerve is the largest sensory nerve branching from the femoral nerve. It travels medially through the adductor canal, or Hunter's canal, bordered by the vastus medialis, abductor longus, and adductor magnus muscles. Entrapment of the saphenous nerve most commonly occurs at the outlet of the adductor canal as the nerve pierces the fascia between the sartorius, vastus medialis, and adductor magnus muscles. While injury to the saphenous nerve from surgery is reported as high as 50-70%, it is reported that less than 1% of adults presenting with lower extremity pain have saphenous neuropathy. Our case series demonstrates successful treatment of compressive saphenous neuropathy from saphenous nerve release. Four patients had complete symptom resolution while another 3 had modest improvement following surgery.

Conclusions: Saphenous nerve entrapment is likely an unrecognized cause of medial knee and lower extremity pain. A history of surgery involving the knee prior to symptom onset or persistent symptoms in spite of surgery likely contributes to the diagnosis of saphenous neuropathy.

Mendez, Joe

Association between Treatment-Related Lymphopenia and Overall Survival in Elderly Patients with Newly Diagnosed Glioblastoma

Abstract:

Background: Management of patients with glioblastoma (GBM) often includes radiation (RT) and temozolomide (TMZ). The association between severe treatment-related lymphopenia (TRL) after the standard chemoradiation and reduced survival has been reported in GBM patients with the median age of 57. Similar findings were described in patients with head and neck, non-small cell lung, and pancreatic cancers. This retrospective study is designed to evaluate whether elderly GBM patients (age ≥65) develop similar TRL after RT/TMZ and whether such TRL is associated with decreased survival.

Methods: Serial total lymphocyte counts (TLC) were retrospectively reviewed in patients (age ≥65) with newly diagnosed GBM undergoing RT/TMZ and associated with treatment outcomes.

Results: Seventy-two patients were eligible: median KPS 70, median age 71 years (range 65 – 86) with 56% of patients >70 years, 53% female, 31% received RT ≤45 Gy. Baseline median TLC was 1100 cells/mm3 which fell by 41% to 650 cells/mm3 two months after initiating RT/TMZ ($p<0.0001$). Patients with TLC <500 cells/mm3 at 2 months had a shorter survival than those with higher TLCs with a median overall survival of 4.6 vs 11.6 months, respectively. Multivariate analysis revealed a significant association between TRL and survival (HR 2.76, 95%CI: 1.30-5.86, $p=0.008$).

Conclusions: Treatment-related lymphopenia is frequent, severe, and an independent predictor for survival in elderly patients with GBM. These findings add to the body of evidence that immunosuppression induced by chemoradiation is associated with inferior clinical outcomes. Prospective studies are needed to confirm these findings suggesting that immune preservation is important in this cancer.

Mitchell, Kyle

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

Kyle Mitchell1, Scott Norris1, Samer Tabbal7, Joshua Dowling2, Keith Rich2, Joel Perlmutter1,3,4,5,6, and Mwiza Ushe1

Departments of Neurology1, Neurological Surgery2, Radiology3, Neuroscience4, Program in Physical Therapy5 & Program in Occupational Therapy6 Washington University School of Medicine, St. Louis, Missouri, USA. Department of Neurology7 American University of Beirut, Beirut, Lebanon.

Abstract:

BACKGROUND: Subthalamic nucleus deep brain stimulation (STN DBS) is an effective treatment for moderate to advanced Parkinson Disease (PD). Studies have shown improvement of motor function and quality of life, but often exclude patients older than 75 years.

METHODS: 91 patients (45>75 years old, 46<75 years old) with STN DBS were retrospectively analyzed. Primary outcome measures were changes in Unified Parkinson Disease Rating Scale subscales III and IV (UPDRS III and IV) at 6 months and 1 year after surgery compared to pre-surgical evaluation. Secondary outcome measures were changes in UPDRS I and II subscales and daily levodopa equivalents. DBS related complications were evaluated.

RESULTS: In the older cohort, STN DBS improved UPDRS III at 6 months (mean + SD) (38.7% 21.8%) and 1 year (36.7% + 28.2%) as well as UDPRS IV at 6 months (-1.2 + 1.9 points) and 1 year (-1.3 + 1.7 points). There were no significant differences in improvement between the two cohorts. Both cohorts had similar worsening in UPDRS I at 1 year, no change in UPDRS II, and similar medication reduction. There were similar numbers of device infections (2/46 and 1/45) and lead malfunctions (1/46 and 2/45). Two patients in the older cohort suffered postoperative intracerebral hemorrhages.

CONCLUSIONS: STN DBS provides similar dramatic motor benefit and reduction in dyskinesia and medications in younger and older patients. In our cohort, older patients had a higher incidence of hemorrhage, though the risk was relatively low. DBS remains effective regardless of age.

Morris, Stephanie

Findings and Serial Neuroimaging in Patients with Linear Scleroderma en Coup de Sabre (ECDS) and Parry-Romberg Syndrome (PRS)

Stephanie M. Morris MD, Rebecca Prengler MD, Andrew White MD, Susan Bayliss MD, and Soe Mar MD

OBJECTIVE: To describe the evolution of neurologic symptoms and neuroradiologic findings in patients with ECDS and PRS.

METHODS: The medical records database at St. Louis Children's Hospital was searched to identify patients diagnosed with "linear scleroderma" who had been evaluated by Rheumatology, Dermatology or Neurology between 1999 and 2015. Each chart was initially reviewed to identify children who had been diagnosed with ECDS or PRS. The resulting charts were then reviewed to characterize skin manifestations, identify associated neurologic symptoms and evaluate for neuroradiologic abnormalities.

RESULTS: 15 patients with ECDS or PRS were identified. Mean age of cutaneous lesion onset was 7.5 years (0-16 years). 14 patients had brain MRI performed, with serial brain MRI available in 7 patients (50%) over an average of 3 years (1-4 years). Of the 14 patients, 6 had abnormal MRI findings which were ipsilateral to the cutaneous lesion in 5 patients. The most common findings were T2/FLAIR white matter hyperintensities (83%). Brain lesions remained stable in 4 patients (80%), while 1 patient had progression in the setting of non-compliance with mycophenolate mofetil, which restabilized with compliance. All patients with abnormal imaging had neurologic symptoms, including migraines (67%), developmental delay (50%), seizures (33%) and facial palsy (17%).

CONCLUSIONS: Unilateral and commonly ipsilateral T2/FLAIR white matter hyperintensities were the most common neuroradiologic abnormalities identified. Lesions remained stable or improved over time with treatment. All patients with abnormal imaging had neurologic symptoms. Our results emphasize that patients with ECDS or PRS would benefit from serial neuroimaging, neurocognitive testing and ongoing neurologic follow-up.

Morris, Stephanie

NF1 gene mutations engender the full spectrum of autism

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IMPORTANCE: A number of published reports describing modest-sized samples of NF1 patients have suggested an elevated autistic trait burden engendered by this monogenic condition. Establishing NF1 as a specific cause of autism spectrum disorder (ASD) and characterizing unique manifestations of ASD in NF1 have critical implications for affected patients and for ongoing research on convergent pathogenic mechanisms that represent potential treatment targets for ASD.

OBJECTIVE: To estimate and characterize the clinical ASD burden in a pooled NF1 data set.

METHODS: This study utilized anonymized, individual-level primary data pooled from six tertiary referral centers in the United States, Belgium, United Kingdom and Australia. 532 individuals age 2.5 – 84 years were recruited from NF1 clinical centers at the respective institutions. Main outcomes included the distribution of ASD (Social Responsiveness Scale) and ADHD (Conners' ADHD Rating Scales) traits, proportion of respective samples meeting conservative cut-offs for clinical ASD, factor structure derived from mixed models analysis, and within-family association of quantitative ASD burden.

RESULTS: 39.2% of individuals with NF1 had SRS-2 scores consistent with clinically-relevant ASD symptomatology (T-score ≥60), while 13.2% had SRS-2 scores strongly associated with a clinical diagnosis of autism (T-score ≥75). The male-to-female prevalence ratio was markedly attenuated (1.6:1) in comparison to idiopathic autism, and mixed models analysis of SRS scores –which exhibited a unitary factor structure-- was suggestive of separable populations of ASD-affected and unaffected individuals in NF1. The association in quantitative autistic trait burden between first degree relatives with NF1 (ICC=0.75) far exceeded that observed in general and idiopathic ASD clinical populations. ADHD prevalence based on published clinical cutoffs was estimated at 45.5%.

CONCLUSIONS: This study establishes NF1 as a common monogenic cause of elevated autistic trait burden, including a prevalence of clinical level affectation one order of magnitude greater than general population risk. This specific cause of ASD features an attenuated sex ratio and a high degree of mutational specificity (inferred from a replication of pronounced familiality in this data set). Collectively, this pooled data set from six NF1 centers underscores the importance of identifying and addressing clinical symptomatology of both ASD and ADHD in patients with NF1.

O'Keefe, Elizabeth

The puzzling case of a 66-year-old woman with a progressive, longitudinally extensive, tract specific, myelopathy

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Abstract: 66-year-old woman presented with progressive pain and sensory deficits attributable to posterior myelopathy of unclear etiology. Spinal cord magnetic resonance imaging showed a longitudinally extensive T2-hyperintense lesion of the dorsal columns. Comprehensive serum, urine, and cerebrospinal fluid analysis failed to identify an etiology. Empiric intravenous methylprednisolone and intravenous immunoglobulin were of no benefit and serial screens for an occult malignancy were negative. She developed dysesthesias and allodynia affecting her entire body and lost the use of her arms and legs due to severe sensory ataxia. She opted against additional aggressive medical management of her condition and passed away on hospice eleven months after symptom onset. Autopsy revealed findings most consistent with polyphasic spinal cord ischemia affecting the dorsal and lateral white matter tracts and, to a lesser extent, adjacent gray matter. The underlying etiology for the progressive vasculopathy remains unknown. Spinal cord ischemia affecting the posterior spinal cord is rare and to our knowledge this case represents the only instance of a progressive dorsal column myelopathy attributable to chronic spinal cord ischemia.

Ong, Charlene

Early Withdrawal Decision Making in Patients with Coma after Cardiac Arrest: A Qualitative Study of Intensive Care Clinicians

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Introduction: Prognostication of patients with coma after cardiac arrest is a task that has traditionally fallen to neurologists. However these patients are more typically under the care of non-neuro intensivists and it is their understanding of prognostication that will influence decisions regarding withdrawal of life-sustaining interventions (WLSI). We observed that the factors that lead to these decisions vary widely, and we considered whether they could result in self-fulfilling prophecies and early WLSI. We conducted a hypothesis-generating qualitative study to identify factors used by non-neurologists to define prognosis in these patients and construct an explanatory model for how early WLSI may occur.

Methods: This was a single center qualitative study of intensivists who cared for cardiac arrest patients with hypoxic-ischemic coma. A total of 30 attendings (n=16) and fellows (n=14) from cardiac (n=7), medical (n=6), surgical (n=10) and neuro (n=6) intensive care units underwent semi-structured interviews after reading hypothetical vignettes. Vignettes were chosen to demonstrate patients with poor neurologic exams at early time points to provoke discussion regarding the circumstances under which early WLSI was acceptable. Questions asked included: What is your feeling regarding prognosis for this patient? How would you frame your discussion with the family? Would you feel comfortable WLSI on this patient at this point? What time frame do you feel is early WLSI for you? Under what circumstances do you feel early WLSI is appropriate? The primary author conducted all interviews. Consolidated criteria for reporting qualitative research (COREQ) was completed. Interview transcripts were analyzed using grounded theory techniques.

Results and Discussion: In this study, the components of early WLSI among non-NICU clinicians appeared to include: 1) Development of fixed negative opinions; 2) Early framing of poor clinical pictures to families; and 3) Shortened time windows for judging recovery potential. The rate of those typically willing to WLSI prior to 72 hours was comparable to other studies citing early WLSI prevalence of 28-63% (1-3).

Therapeutic hypothermia appeared to lengthen the period of observation, but in many cases did not change negative opinions for non-NICU physicians. Physicians from all specialties drew conclusions using a constellation of factors, some of which differed from those traditionally recommended by neurologic guidelines to inform their prognostications. Non-NICU physicians weighted CPR circumstances and the absence of signs of consciousness more heavily than NICU physicians. NICU and non-NICU physicians similarly weighted age and baseline comorbidities. Because non-NICU physicians are not trained in the methodology that leads to neurologic prognosis, they may be more likely to seek early evidence of consciousness to assure themselves of recovery potential, and more likely to be discouraged in its absence. These data also suggest that the self-fulfilling prophecy is a group process. While the high prevalence of early fixed opinions and willingness to withdraw care among trainees compared to attending physicians may reflect a lack of experience with unexpected outcomes, and a desire to streamline the workflow within the ICU setting, it may set the stage for early WLSI decisions made by the group.

Conclusions: Elucidating the framework primary ICU physicians employ when considering early WLSI is important to inform how consulting neurologists should approach their colleagues in cases of coma after cardiac arrest. Targets for education include reinforcing that lack of consciousness within the first 72 hours does not preclude good outcome, measured family discussions, and encouraging a 72 hour observation window. Further study should be conducted to examine the generalizability of these results.

Silbermann, Elizabeth

Retinal Nerve Fiber Layer Thinning, Balance, and Disability: A Pilot Study

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Background: Retinal imaging has been proposed as a fast, quantitative measure of global disease in multiple sclerosis. Balance impairment can be an early complication of relapsing remitting multiple sclerosis (RRMS) which can be associated with decreased ambulation and disease progression.

Objectives: Assess the relationship between retinal thinning and standing postural control to determine whether the retina can serve as a biomarker for balance and ambulation.

Methods: 27 RRMS subjects participated in this cross sectional study. Patients' neurologic disability was assessed using expanded disability status scale (EDSS). Balance and gait parameters were evaluated using APDM Opal Body-Worn Sensors using the Instrumented Sway Test (ISway). Mobility Lab Software was used to calculate specific variables of standing postural control including range of acceleration and jerk (sway smoothness). Patients underwent spectral domain ocular coherence tomography assessment to obtain retinal nerve fiber layer thickness as well as macular volume.

Results: Spearman's rho two-tailed correlations were used to evaluate relationships between OCT, EDSS and postural control measures. A moderate correlation was observed between central RNFL thinning and EDSS (ρ=-0.429, p=0.013). Mild to moderate correlations were demonstrated in MS patients in normalized jerk with eyes open on an unstable surface (foam pad) and RNFL thinning in the following areas: central (ρ=-0.362, p=0.001), nasal inferior (ρ=-.338, p=0.002), temporal inferior (ρ=-0.320, p=0.004), and temporal (ρ=-0.222, p=0.050) quadrants.

Conclusions: Early results of this pilot study demonstrate a correlation between retinal thinning and normalized jerk with eyes open on unstable surface. This suggests that retinal thinning may serve as a biomarker for balance deficits in people with MS.

White, Michael

Pseudoprogression versus Progression on Gadolinium-Enhanced MRI in Oligodendrogliomas and Mixed Oligoastrocytomas

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Abstract: Pseudoprogression is a radiological phenomenon in which tumors develop new areas of contrast enhancement in the 6 months following chemoradiotherapy that is often difficult to distinguish from true disease progression. We hypothesized that in Oligodendrogliomas (OG) and Mixed Oligoastrocytomas (MOA) new early contrast enhancement on MRI was unlikely to be associated with true tumor progression. We retrospectively identified 11 patients with either OG or MOA who had new areas of contrast enhancement and underwent second-look surgery within 6 months of receiving radiation with or without chemotherapy. Among these patients, there were no cases of progression to a higher grade, 9 of 11 had greater than 50% radiation necrosis with 5 have more than 80% necrosis. Within this group 4 underwent sub-total resection, 4 had gross-total resection, and 3 had biopsy only. We also identified 14 patients who developed new enhancement more than 6 months following radiation completion. Within this group, 8 of 14 progressed to a higher grade and only 2 demonstrated pseudoprogression. Notably, second-look surgery was associated with significant morbidity. Our findings support the hypothesis that early contrast enhancement following chemo-radiotherapy is frequently pseudoprogression.