Washington University
School of Medicine
Department of Neurology

Residents' Day Symposium
Friday, May 12, 2017
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.

Albertson, Asher

Potential Role of Axonal Sprouting in Cortical Remapping and Recovery of Functional Connectivity after Focal Ischemia

Asher J. Albertson, Andrew W. Kraft, Quingli Xiao, Jin-Moo Lee

Focal ischemia results not only in infarction of a brain region, but in disconnection of that region from the global brain network. In the case of focal cortical ischemia, this is characterized by diminished activity in the region of the infarct, as well as disrupted whole brain functional connectivity (FC). Subsequent recovery is also associated with significant changes in local circuit activation as function lost to the infarction "remaps" to adjacent cortex. Additionally, global network function typified by whole cortex functional connectivity normalizes. While functional imaging studies have consistently demonstrated both of these changes, it is unknown if these paired processes are necessary for behavioral recovery. Furthermore, the underlying structural substrate is poorly understood. Our lab has shown that remapping and restoration of FC is dependent on synaptogenic mechanisms, however it is unclear if new axons sprout to mediate these connections or if pre-existing circuits simply alter their existing synaptic activation, independent of any structural reorganization. It is our hypothesis that recovery from stroke is dependent on both local circuit remapping and global network reintegration, and that these changes in functional anatomy reflect newly formed circuits resulting from new axon sprouting. We employ stimulus-evoked optical intrinsic signal (OIS) imaging to examine local circuit remapping, as well as the novel technique of functional connectivity OIS imaging to study global network re-integration in mice with focal somatosensory strokes. To examine the role of thalamocortical axon sprouting in recovery from somatosensory stroke, we have generated an shRNA targeting Growth Associated Protein 43 (GAP43), a protein critical to axon sprouting which is significantly upregulated following stroke. Using stereotactic thalamic injections and viral gene transfer we are able to significantly decrease thalamic GAP43 protein expression. Serial imaging of stimulus evoked remapping and whole brain functional connectivity is then performed while concurrently quantifying behavioral recovery. Future work will examine a possible role for local cortical and transcallosal axon sprouting in stroke recovery by targeting GAP43 shRNA to the peri-stroke and contralateral cortex.

Basit, Areeba

Predictors of relapse and short term disability in pediatric patients with relapse-onset Multiple Sclerosis (MS) on immunomodulatory therapy

Areeba Basit, Jenny Wang, Tiffany Lin, Emily Egbert, Allysa Lui, Marvin Petty, Nova Olgak, Amber Salter, Soe Mar

OBJECTIVE: To identify predictors of relapse and short term disability in pediatric patients with relapse-onset MS.

BACKGROUND: MS is a recurrent inflammatory disease that can cause progressive neurologic dysfunction. It is important to recognize factors that may contribute to worsening outcomes.

METHODS: Patients with onset of MS before 18 years of age who had routine follow-up and an Expanded Disability Status Scale (EDSS) score at each visit, were identified between 2002 and 2016. Information on their disease course including duration, relapses and MRI lesion burden was obtained through chart review. Logistic regression was used to evaluate the risk of having a relapse for the predictors of interest during the first assessment. Generalized estimating equations (GEE) models that take into account repeating events, were used to evaluate the risk of having a relapse for different factors. Linear regression was used to evaluate predictors of EDDS change from baseline to end of 3 years. All tests were two-sided and a significance level of 0.05 was considered significant.

RESULTS:
Predictors of relapse:
43 patients were included in the analyses of which 72% were females with the mean age at diagnosis being 16 years. The younger the age at diagnosis, higher the risk of relapse (p=0.0112). Adjusting for age, higher EDSS scores at baseline are associated with a 2.4-fold increased risk of having a relapse (p=0.0259). This effect persists when you also control for the type of DMT during first year of diagnosis. There is an increased risk of having a relapse associated with increasing EDSS score (p=0.0384), increasing number of T2 (p=<0.001) and T1 lesions (p=0.002). After controlling for EDSS score, the number of T2 lesions is associated with increased odds of having a relapse (p-0.0324). For every 5 lesion increase in T2 lesions, there is a 4% increased risk of having a relapse.

Predictors of short term disability:
24 patients were included in the analyses of which 79% were females with mean age at diagnosis being 16.2 years. The remaining 19 patients did not have a full 3 year follow up completed. Baseline EDSS predicts change in EDSS score over 3 years. Lower EDSS score at baseline predicts improvement in EDSS change over 3 years (p=<0.0001). Gap in time from diagnosis to starting DMT predicts change in EDSS score over 3 years. Increasing gap in time predicts increasing change in EDSS (p=0.0366).

CONCLUSIONS: Our results add to the limited knowledge of predictors of disability in Pediatric MS. Identifying these factors can help with earlier and more aggressive implementation of therapies.

Evans, Emily

A review of the role of diet and nutrition in multiple sclerosis

Emily Evans, Anne Cross, and Laura Piccio

Abstract: Multiple Sclerosis (MS) is a chronic inflammatory disorder of the central nervous system. Despite the availability of many disease modifying therapies patients with MS still experience persistent symptoms and disability, which could be mitigated by adjunctive therapies. Adjunctive therapies need not be limited to pharmacological compounds, but can also include lifestyle modifications. One interesting, underexplored area of potential adjunctive therapies in MS is dietary and nutritional interventions. Surveys suggest that over half of MS patients are already utilizing some form of dietary manipulation and that over three-quarters would be interested in participating in clinical trials in diet and nutrition. Many dietary interventions and supplements have been preliminarily explored in MS. This paper aims to provide a comprehensive overview of the current state of evidence for the role of diet and nutrition in multiple sclerosis including the scientific rationale and biological plausibility for each supplement's utility in MS, possible harms and safety issues of each supplement, a review of the current state of evidence from animal and human trials of each supplement in MS, and further directions for exploration and important unanswered questions in the field.

Findlay, Andrew

The Role of DNAJB6 In Muscle And The Impact Of LGMD1D Mutations

Abstract: Dominant missense mutations in DNAJB6 cause LGMD1D, a disorder characterized by adult onset slowly progressive proximal weakness and muscle biopsy with rimmed vacuoles and protein aggregates. The role of DNAJB6 in muscle and how LGMD1D mutations result in muscle pathology and weakness remain unclear. To understand this, we explored the role of DNAJB6 and its disease mutations in myoblasts, differentiated skeletal muscle and human iPSC derived cardiomyocytes. Surprisingly, loss of DNAJB6 in myoblasts leads to enhanced myoblast fusion, differentiation, and myotube size via enhanced WNT/B-catenin signaling. In contrast DNAJB6 disease mutations suppress WNT/B-catenin and inhibit myoblast fusion and differentiation. In addition, absence of DNAJB6 leads to an accumulation of sarcomeric proteins that aggregate in myotubes. To further explore this, we performed live in vivo imaging of mouse skeletal muscle using two photon fluorescence microscopy. These studies demonstrated distinct differences in baseline DNAJB6 sarcomeric localization and its dynamic recovery at the Z disc compared to DNAJB6 with disease mutations. Future studies will utilize human iPSC derived cardiomyocytes to understand DNAJB6's impact on both WNT/B-catenin signaling and sarcomere assembly in a relevant human model.

Griffith, Jennifer

Magnesium sulfate and ziprasidone as treatments for pediatric status migrainosus

Jennifer L. Griffith, M.D., Ph.D., Nausheen Hasan, PharmD, and Soe Mar, M.D.

OBJECTIVE: Evidence for the use of atypical agents in treatment of acute headache is limited. This study aimed to evaluate the efficacy and safety of magnesium sulfate (MgSO4) or ziprasidone (ZPS) as treatments for pediatric status migrainosus.

METHODS: The medical records database at St. Louis Children's Hospital was searched to identify all patients receiving MgSO4 or ZPS in the ER or inpatient setting between February 2013 and February 2016. Patients with diagnosis of headache were included in the dataset. Charts were reviewed for patient characteristics and treatment response.

RESULTS: Twenty-seven patients received IV MgSO4 (dose range 500 mg – 2000 mg). Median duration of headache prior to presentation was 10 days. Fifteen of 27 patients had received at least 2 medications prior to MgSO4. Change in headache severity (on 10-point scale) was 3.3 ± 3.5 (mean ± st. dev.). Only two patients had adverse effects of MgSO4 (abdominal pain; mild elevation of serum Mg [2.8 mg/dl]). Three patients received IM ZPS (dose range 10 – 20 mg). All patients had received at least 3 medications prior to ZPS. Only 1/3 patients had improvement in headache at discharge. No adverse effects of ZPS were reported.

CONCLUSIONS: Evidence regarding use of IV MgSO4 for treatment of acute headache is mixed, however in this retrospective chart review IV MgSO4 was not an effective abortive treatment for pediatric migraine. Although a recent study suggests IM ZPS may be effective for status migrainosus in adults, our limited data do not suggest it is effective in adolescents.

Griffith, Jennifer

T2 Hyperintensities in Children with Neurofibromatosis Type 1 (NF1)

Jennifer L. Griffith, M.D., Ph.D., Jasia Mahdi, M.D., Stephanie Morris, M.D., Manu Goyal, M.D., David Gutmann, M.D., Ph.D.

OBJECTIVE: NF1 patients develop low-grade brain tumors in optic pathway and brainstem. MRI also shows T2 hyperintense lesions (T2H) throughout the brain. We aimed to characterize the prevalence, location and natural history of T2H in children with NF1

METHODS: We reviewed a cohort of 170 children with diagnosis NF1 evaluated clinically at SLCH. MRIs obtained at SLCH between 2006 and 2016 were included in the analysis. The number, location and characteristics (border, shape, and degree of associated T1-hypointensity, contrast enhancement and mass effect) were recorded.

RESULTS: MRIs of 40 patients were reviewed in this preliminary analysis. Ten patients (25%) had a single MRI, while the remainder had at least 1 serial scan. Among patients with serial scans, median interval between 1st and last scan was 5.5 yrs. All patients had at least one T2H on at least one MRI. Young children tended to accumulate T2H, and T2H tended to resolve in teenage years. The most commonly identified locations were cerebellar white matter (82% patients), globus pallidus (68%), thalamus (63%), medial temporal lobe (58%), brainstem (53%), periaqueductal region (34%), and subcortical white matter (32%). The percent of T2H meeting radiographic criteria for low-grade glioma varied by location.

CONCLUSIONS: T2H are found throughout the brain, brainstem, and cerebellum. Many T2H have radiographic characteristics of low-grade glioma, yet the majority of T2H remain stable or resolve with age. Further studies are needed to identify the clinical significance of T2H.

Hartman, Jeremy

DBS for Parkinson's disease induced focal dystonia treated with Onabotulinumtoxin A

Intro:
Focal upper limb dystonia is an uncommon cause of disability with a prevalence of all dystonia of 1 in 2500. While dystonia is now being treated by the placement of deep brain stimulators (DBS), DBS as a cause of dystonia is very uncommon. This case looks at the treatment of post DBS placement related focal upper extremity dystonia with onabotulinumtoxin A.

Case:
This patient is a 40-year-old woman with a history of Parkinson disease diagnosed at 35 years of age. She underwent DBS placement in 2014 for rigidity. After the time of her DBS placement she developed left hand and wrist extensor dystonia and CRPS type II. Despite initial treatment for her CRPS with Stellate ganglion blocks she continued to have dystonia. She was referred to a hand surgeon and underwent A1 pulley release and FDS tenotomy to the left long and ring fingers in 2016 without resolution of her hand dystonia. She was referred for the ongoing management of her focal left upper extremity dystonia with Botox. Her first treatment in 12/2016 she received 200 units of Botox divided amongst her left wrist and finger extensors, lumbricals/interossei, and FDS for which she reported excellent results with improved left hand control and ability to perform ADLs. She reported that her symptoms improved so much that she trialed returning to work in February 2017, however, due to cognitive fatigue from her ongoing Parkinson's disease she has not been able to continue. She continues to receive Botox roughly at 3 month intervals with excellent responses.

Discussion:
Focal dystonia after DBS placement in Parkinson's disease is an uncommon consequence following the treatment of movement disorders and can be difficult to treat (3). There is a single case report from Gupta et al in 2016 that described a case series of 6 patients with focal foot dystonias following DBS placement with Botox who likewise had excellent results (1). There are numerous difficulties in quantifying the success of dystonia treatment due to the lack of validated scales to measure symptoms severity (2).

1. Torres-Russotto, Diego, and Joel S. Perlmutter. "Focal Dystonias of the Hand and Upper Extremity." The Journal of Hand Surgery 33.9 (2008): 1657-658. Web.

2. Gupta, A., and R. Visvanathan. "Botulinum toxin for foot dystonia in patients with Parkinson's disease having deep brain stimulation: A case series and a pilot study." Journal of Rehabilitation Medicine 48.6 (2016): 559-62. Web.

3. Baizabal-Carvallo, José Fidel, and Joseph Jankovic. "Movement disorders induced by deep brain stimulation." Parkinsonism & Related Disorders 25 (2016): 1-9. Web.

Justmann, Jessica

Recovery from Paraplegia Following Epidural Steroid Injection

Introduction: In this case, we present a patient with sudden onset bilateral lower extremity weakness and urinary retention following epidural steroid injection. Epidural steroid injections are a mainstay of conservative treatment of back pain with radicular symptoms. Common side effects include vasovagal response, flushing, back ache and postural headache1. There are rare reported cases of conus medullaris infarct following epidural steroid injection2. There are even rarer incidences of drug related myelitis following epidural steroid injection3.

Case description: LL is a 35 year old male with chronic back pain due to a motor vehicle collision who was undergoing epidural steroid injection when he experienced severe pain causing him to thrash. He noted subsequent sudden onset weakness of the bilateral lower extremities as well as numbness of the buttocks, genitals and lower extremities. He underwent MRI of his spine which demonstrated T2 hyperintensity from T11-12 through the conus medullaris. He was diagnosed with acute infarct vs drug related myelitis of the conus medullaris. He was admitted to acute inpatient rehabilitation. At the time of transfer to acute inpatient rehabilitation he continued to require intermittent catheterization, BERG 4, transfers 50% assist, grooming and lower extremity dressing 50% assist, and was not able to ambulate. Over the course of his rehabilitation he was treated with E-stim, gait training, strengthening and bracing. At the time of discharge he was able to ambulate with kinesiotape for knee and ankle stabilization and bilateral AFOs. He was continent of bowel and bladder and voiding spontaneously. He was able to be discharged to home and the care of his family.

Discussion: A single case of drug related myelitis was found in literature search and occurred in a patient with Bechet's disease3. Prior case reports of infarct of the conus medullaris are more frequent but do not address treatment modalities used2. Outcomes reported vary from persistent paraplegia to complete resolution of mild weakness2. In this case we discuss the recovery of a patient with paraplegia as well as the possible differentiation of the diagnosis.

1. Gharibo CG et al. Conus Medullaris Infarction After a Right L4 Transforaminal Epidural Steroid Injection Using Dexamethasone. Pain Physician. 2016 Nov-Dec;19(8):E1211-E1214.

2. Ryan D. Tackla, et al. Conus medullaris syndrome after epidural steroid injection: Case report. Int J Spine Surg. 2012; 6: 29–33.

3. Deshpande DM, Krishnan C, Kerr DA. Transverse myelitis after lumbar steroid injection in a patient with Behcet's disease. Int J Spine Surg. 2012; 6: 29–33.

Kharod, Rucha

Botox Application for Recurrent Wrist Pain: A Case Report

Case Description: 1-year-old female swimmer developed progressively worsening dominant wrist pain during swim season 2.5 years ago, exacerbated with activities such as typing and gripping. During the first year, multiple imaging studies were inconclusive. Conservative analgesia and wrist splinting were unsuccessful in improving pain and hand function. At 1 year, the orthopedic diagnosis of Flexor Carpi Radialis (FCR) tendonitis was addressed with peritendinous FCR steroid injection, but pain recurred within 6 months. Next, partial thickness Triangular Fibrocartilage tear with wrist effusion was diagnosed with MRI. Wrist arthroscopy with debridement did not result in lasting relief either. The patient was then offered FCR tenotomy versus surgical excision, which she declined.

At 2 years, this patient was evaluated by Rehabilitation medicine in an outpatient setting.

The patient was diagnosed with focal dystonia of FCR with Writer's cramp. 50U of intramuscular Botulinum toxin A was injected into the FCR, Flexor-Pollicis-Longus, and Flexor-Digitorum-Superficialis, followed by rehabilitation with specialized hand therapy. The patient reported gradual improvement, with resolution of symptoms in 4 weeks.

Results: The patient was diagnosed with focal dystonia of FCR with Writer's cramp. 50U of intramuscular Botulinum toxin A was injected into the FCR, Flexor-Pollicis-Longus, and Flexor-Digitorum-Superficialis, followed by rehabilitation with specialized hand therapy. The patient reported gradual improvement, with resolution of symptoms in 4 weeks.

Conclusions: A high index of suspicion for FCR focal dystonia should exist for persistent wrist pain that has failed conservative and surgical management for other diagnoses. Botox has merit for use as both a diagnostic and therapeutic tool for FCR dystonia. Further study can help in establishing evidence for this treatment method.

Landsness, Eric

Genetically-encoded calcium indicators (GECI) in mice to monitor whole-cortex activity during sleep, anesthesia and wakefulness

Landsness, EC , Brier LM, Wright PW, Bauer AQ, Lee, JM, Culver JP

Introduction: A hallmark of non-rapid eye movement (NREM) sleep is the anterior to posterior propagation of slow waves (0.5-4.5 Hz). However, the network basis 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 sleep and compare them to anesthesia sedation and 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, sleep, dexmedetomidine and ketamine anesthesia with simultaneous EEG collection.

Results: There is a significant increase in the spectral content of the GCAMP signal in the delta range over the motor, somatosensory, and visual cortices under sleep and anesthesia compared to wakefulness. 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. Functional connectivity (FC) analysis showed a transition from a correlative pattern that was binary along the anterior-posterior axis during sleep and anesthesia to a more complex, local connectivity pattern seen in wakefulness.

Conclusions: OIS imaging of GCaMP mice provides repeatable, non-invasive, 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.

Loftspring, Matthew

Early Improvement in Collateral Flow after Acute Ischemic Stroke is Associated with Larger Penumbral Signature and Improved Clinical Outcomes

Matthew C. Loftspring, MD, PhD1, Cihat Eldeniz, PhD2, Weili Lin, PhD3, Andria L. Ford, MD1, Hongyu An, PhD2, and Jin-Moo Lee, MD, PhD1,2

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Abstract: Good collateral flow is postulated to play an important role in maintaining tissue viability and conferring good outcome after acute ischemic stroke (AIS). However, it is unclear if collateral flow is a dynamic process early after AIS, and whether early changes influence outcomes. In this study we analyzed prospectively obtained clinical data and serially-acquired multi-modal MR images from 50 patients with AIS involving the middle cerebral artery. Dynamic susceptibility contrast-enhanced (DSC) and apparent diffusion coefficient (ADC) sequences were acquired at <4.5h, 6h and 24h after stroke onset; additional FLAIR images were obtained at 1 month. Serial NIHSS assessments were obtained at each time-point and mRS was collected at 90d. Collateral flow was graded using an angiographically-validated DSC methodology, generating a semi-quantitative scale ranging from 1 to 4 (higher numbers representing more robust collateral flow). Collateral flow was dynamic within the first 24 hours: 33% of patients had improvement in collateral grade between <4.5h to 24h, while 67% had either worsening or no change. Patients with better collateral flow at <4.5h had better tissue outcomes as measured by relative infarct growth (69% of at-risk brain volume went on to infarct vs 42%; p=0.029). Among patients with a good outcome (mRS 0-2), 63% had improvement in collateral flow and, among those with a poor outcome (mRS 3-6), 10% had improvement (p=0.04). These results suggest that collateral flow after AIS is dynamic and that early improvement in collateral flow is associated with enhanced tissue and clinical outcomes.

Long, Justin

Sensitivity and Specificity of CSF VZV Antibody and PCR Testing in Suspected VZV Vasculopathy

Justin Long, James Giles, Lynn Zhang, Peter Kang, Laura Baldassari, Kristen (Gehrking) Andruska, Carey-Ann Burnham, Craig Wilen, Beau Ances, Robert Bucelli.

Background: Vasculopathy due to varicella zoster virus (VZV) infection is a secondary cause of stroke in patients with zoster reactivation, with or without rash. A limited series of previous studies in patients with VZV vasculopathy have demonstrated a significantly increased sensitivity when testing for the presence of CSF anti-VZV IgG as compared to CSF VZV DNA via PCR. However, there is limited independent verification of this finding and lack of evidence as to the specificity of anti-VZV IgG antibodies in CSF of patients without VZV, most crucially in those with strokes not related to VZV infection.

Goal: To assess the sensitivity and specificity of CSF anti-VZV IgG and CSF VZV DNA testing by PCR, both in isolation and in combination, in patients with suspected VZV vasculopathy.

Methods: We prospectively identified and collected blood and CSF specimens from 9 control subjects without stroke, 20 disease control subjects with stroke unrelated to VZV infection and 6 subjects with stroke due to suspected VZV vasculopathy (i.e. stroke either with active or recent history of zoster rash). Prior to CSF analysis, patients were assigned to these groups on clinical grounds using pre-defined criteria. Specimens were analyzed for VZV DNA copies by PCR and anti-VZV IgG and IgM levels.

Results: Among 6 patients with suspected VZV vasculopathy, 3 (50%) had CSF VZV DNA and 4 (67%) had CSF anti-VZV IgG. Among 20 patients with stroke due to other causes, 0 patients had CSF VZV DNA and 1 had CSF anti-VZV IgG. Among 9 patients without stroke, 0 had CSF VZV DNA or anti-VZV IgG. For presence of CSF VZV DNA alone, sensitivity/specificity for detection of VZV vasculopathy was 50%/100%. For presence of CSF VZV anti-IgG alone, sensitivity/specificity was 67%/97%. For presence of either CSF VZV DNA or anti-IgG, sensitivity/specificity was 83%/97%. The difference in sensitivity for presence of CSF VZV DNA alone as compared to presence of either CSF VZV DNA or anti-IgG was not statistically significant by McNemar test ($p=0.2482$), although sample size for this comparison was quite small ($n=6$).

Conclusions: The presence of either CSF VZV DNA or CSF VZV anti-IgG is highly specific for VZV vasculopathy. Sensitivity is improved by testing for both VZV PCR and anti-IgG, although sample size was too small in this study to demonstrate statistical significance.

Study supported by: The Paula C. and Rodger O. Riney Fund.

Rudock, Robert

Juvenile Alexander Disease Presenting in a 10-year-old Girl with Chronic Emesis

Introduction: Alexander disease is a rare neurodegenerative leukodystrophy of astrocyte dysfunction, affecting 1 in 2.7 million people. Classification of Alexander disease is based upon age of symptom onset, and diagnosis is based upon neuroimaging, histopathology, and GFAP testing. Despite the known causative gain-of-function mutation, treatment remains supportive.

Case Description: 10-year-old previously healthy and developmentally appropriate girl presented with a 1-year history of worsening emesis. Emesis was non-bloody and non-bilious, worse in the mornings and with activity. Early evaluation demonstrated esophageal candidiasis on EGD (esophagogastroduodenoscopy) with subsequent treatment with fluconazole. Concurrent hematologic and oncologic evaluation, including bone marrow biopsy, was unrevealing. Patient was later admitted to the gastroenterology service for weight loss (12 pounds) secondary to frequent emesis. Brain MRI obtained to evaluate for alternative non-GI etiologies of emesis, which demonstrated an enhancing dorsal medulla lesion, along with symmetric bifrontal white matter lesions. GFAP testing was positive for a known variant, consistent with Juvenile-onset Alexander disease. Patient was subsequently started on IV dexamethasone with improvement in emesis, followed by a transition to oral methylprednisolone.

Discussion: Emesis was likely secondary to enhancing dorsal medulla lesion, involving the area postrema. Steroids may help with emesis and bulbar symptoms. β-lactam antibiotics, including ceftriaxone, may be a potential treatment option; mechanism theorized to decrease glutamate excitotoxicity.

Soleimani-Meigooni, David

Quality of epilepsy documentation and compliance with American Academy of Neurology guidelines in the neurology resident continuity clinic

David N. Soleimani-Meigooni, Brendan Eby, Leanne Stunkel, Maggie Blattner, Gabriela de Bruin, Susan Criswell

Epilepsy is one of the most common neurological problems managed by residents in the outpatient continuity clinic. The American Academy of Neurology (AAN) has well-established quality measures for management of patients with epilepsy. These guidelines were not previously integrated into the resident continuity clinic.

Each resident was asked to review the charts of five epilepsy patients that they had seen during the first-half of the 2016 – 2017 academic year, assessing how well they met the AAN guidelines on a standardized worksheet. This process allowed for resident-directed self-assessment of compliance with epilepsy guidelines. After collection of the initial survey, an electronic medical record template was implemented to help residents quickly and accurately record all of the information that is important for the management of epilepsy patients per the AAN guidelines. After implementation, each resident then reassessed his/her epilepsy patient notes to determine if the documentation improved and if there was better compliance with the guidelines. Data was also collected on the familiarity of the residents with the AAN guidelines before the start of the project and after the intervention was implemented.

In the future, this system will be adapted to implement additional quality of care guidelines in the resident clinic. This will promote knowledge and application of quality of care guidelines in the routine management of common neurological diseases.

Singh, Inder

Association between radiological burden and headache severity

Inderpal Singh MD, Amber Salter, EMILY Wu BS, Soe Mar MD
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Background: The prevalence of headache (migraine in particular) is higher among multiple sclerosis (MS) patients when compared to the general population, with ~50% of MS patients experiencing headaches as adults at MS presentation. [1]

In adult relapsing-remitting MS, patients with migraine presented with a higher mean number of contrast enhancing lesions compared to those without migraine (1.2 vs 0.27) (p=0.02). [2]

Hypotheses regarding how headache results from various forms of MS pathogenesis include decreased serotonin in the cerebrospinal fluid, sympathetic hypofunction, and cytokine changes [3]

Aim of the study: To study the prevalence of headaches in pediatric MS patients.

To study the association, if any, between radiological burden of MS with headache severity which was categorized as less than twice a week (occasional) vs frequent.

Methods: Retrospective chart review of patients from multiple sclerosis database at Saint Louis Children's Hospital, St Louis, MO

N=49, age ranging from 9 to 21 yrs.

Patients with headache reported at the time of MS diagnosis were included

Results: 32 patients (65%) had headaches at the time of pediatric MS diagnosis with confidence interval of 95%.

20 patients (40%) had frequent headaches with MRI showing average of 23.3 supratentorial T2/FLAIR lesions. 12 patients (24%) HA remained occasional with average lesions of 12.4. p value of 0.049 using unpaired t test.

Conclusion: 32 patients (65%) had headaches at the time of pediatric MS diagnosis with confidence interval of 95%.

20 patients (40%) had frequent headaches with MRI showing average of 23.3 supratentorial T2/FLAIR lesions. 12 patients (24%) HA remained occasional with average lesions of 12.4. p value of 0.049 using unpaired t test.

Reference

1. Prevalence of primary headaches in people with multiple sclerosis. D. D'Amico, L. La Mantia, A. Rigamonti, S Mascoli, C. Milanese, G. Bussone. Cephalalgia, 24 (2004), pp. 980–984

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3. Migraine in multiple sclerosis. Int Rev Neurobiol. 2007;79:281–302 Elliott DG.

Stunkel, Leanne

Overdiagnosis of Optic Neuritis

OBJECTIVE: To assess the incidence of, and characterize factors contributing to, overdiagnosis of acute optic neuritis in patients seen by a neuro-ophthalmology service at one tertiary care center.

DESIGN: Retrospective clinic-based cross-sectional study.

METHODS: New patient encounters between January 2014 and October 2016 were retrospectively reviewed to identify patients referred with a diagnosis of acute optic neuritis. Definite diagnosis was determined by fellowship-trained neuro-ophthalmologists. For cases found not to have optic neuritis, the Diagnosis Error Evaluation and Research (DEER) taxonomy tool was applied to identify the type of diagnostic error.

PARTICIPANTS: 122 patients referred for acute optic neuritis to the neuro-ophthalmology clinic at the Washington University School of Medicine in St. Louis.

MAIN OUTCOME MEASURES: The primary outcome measure was the primary type of diagnostic error in patients erroneously diagnosed with optic neuritis. Secondary outcomes included the final diagnosis assigned by the attending neuro-ophthalmologist, and what interventions patients underwent prior to referral.

RESULTS: 122 patients were referred with acute optic neuritis during the study period. 49 (40%) were confirmed to have optic neuritis. 73 (60%) patients had an alternative diagnosis. The most common alternative diagnoses were headache and eye pain, functional visual loss, and other optic neuropathies, particularly non-arteritic anterior ischemic optic neuropathy (NAION).

The most common diagnostic errors were in eliciting or interpreting critical elements of history, 24 of 73 (33%). The second most common were errors weighing or considering alternative diagnoses, 23 of 73 (32%). The next most common were errors weighing or interpreting physical exam findings, 15 of 73 (21%). Other errors were due to misinterpretation of diagnostic tests, 11 of 73 (14%).

In patients who did not have optic neuritis, 12 (17%) had negative MRI results preceding the referral, 12 (17%) had received a lumbar puncture, and 8 (11%) had received inappropriate treatment with IV steroids.

CONCLUSIONS: Optic neuritis was overdiagnosed in 60% of referred patients, prompting unnecessary and costly diagnostic tests, procedures, and treatments. The most common errors were overreliance on a single item of history and failure to consider alternative diagnoses.

Wilks, Anson

Elevated Lipoprotein(a) in a Woman with Complex Aortic Plaque

Wilks AW, Carpenter DA

A 51-year-old woman with a history of hypertension, hyperlipidemia, type 2 diabetes, and stroke two years prior with residual left-sided weakness presented to the ED after having memory difficulties at work. She has a family history of cardiovascular disease including several family members with premature disease. In the workup for her cognitive changes, an MRI was performed that showed multifocal strokes in different vascular distributions. The workup for the etiology of her stroke included a TEE that demonstrated a complex aortic plaque thought most likely to be the etiology for her strokes. In the work up of her family history of early cardiovascular disease and poor response to high-intensity statin therapy as identified by persistently elevated LDL, Lipoprotein(a) level was obtained that was found to be greater than the upper limit of detection based on the assay. Lipoprotein(a) has emerged in recent years as an independent risk factor for cardiovascular disease including stroke. Traditional lipid lowering therapies such as statins have no effect on lowering lipoprotein(a) while niacin has been proven to be successful in lowering levels. (However, the clinical efficacy of this measure has yet to be proven.) Furthermore, aortic atherosclerotic disease has been shown to be associated with stroke and remains a consideration for multifocal strokes for which an intracardiac source has not been determined.

Wooliscroft, Lindsey

Diffusion Basis Spectrum Imaging (DBSI) parameters of acute multiple sclerosis lesions can predict persistent black holes

Abstract: Background and Objective: Around 35% of contrast-enhancing lesions (CELs) in multiple sclerosis (MS) evolve into persistent black holes (PBHs), which have greater axonal loss than non-black holes (NBHs). We previously used diffusion tensor imaging (DTI) parameters to predict PBH formation. Diffusion basis spectrum imaging (DBSI) is the next generation diffusion technique, which models diffusion weighted MR signals as a linear combination of multiple anisotropic diffusion tensors (representing axon fibers and tracts) and a spectrum of isotropic diffusion tensors (representing cells, edema and extracellular water). DBSI resolves the confounding effect of crossing fibers and quantitatively identifies inflammation that confounds DTI interpretation. The purpose of this experiment was to determine if DBSI of CELs can predict the subsequent development of PBHs, which are a surrogate of tissue damage and axonal loss. We also compared DBSI to DTI and Magnetization transfer contrast (MTC).

Methods: 9 RRMS patients with 95 total CELs were imaged monthly on a 3.0T Siemens Trio scanner until enhancement ceased. A region of interest (ROI) representing the CEL was drawn on the T1W postcontrast image at time of maximum contrast-enhancement. DTI, MTC and DBSI-determined parameters were measured at this scan. For fiber fraction and MTC, measures that are volume based, the ROI drawn in the CEL was compared to a mirror ROI drawn on contralateral normalappearing white matter (NAWM). Twelve months later, development of PBH, persistent gray hole (PGH) or NBHs was determined by 2 examiners with a third adjudicator. The results were analyzed using linear hierarchical models of the imaging parameters from lesion to contralateral NAWM (L/C) ratios for fiber fraction and MTC or from lesion ROIs (for other DBSI-derived measures). A summary p-value from each model tests for difference between lesions that became PBHs/PGHs versus NBHs.

Results: Differences in baseline DBSI measures for CELs between those that became PBH/PGH versus NBH were observed. Reduced DBSI fiber ratio ($p=0.044$), reduced AD ($p=0.18$), reduced fiber FA ($p=0.0042$) and increased RD ($p=0.097$) were associated with an increased probability of a CEL becoming a PBH or PGH. Differences between the PGH/PBH and NBH outcomes also existed for DTI and MTC measures at baseline, though the direction of the relationship differed dramatically for DBSI and DTI axial diffusivity. Increased DTI axial ($p=0.0032$), increased DTI radial ($p=0.0022$), decreased DTI FA ($p=0.0098$) and decreased MTC ($p=0.0054$) were associated with an increased probability of a CEL becoming a PBH or PGH.

Conclusions: Based on the earlier animal studies, we had hypothesized that decreased DBSI-derived fiber fraction at CEL onset would be associated with later formation of PBH/PGH, and indeed this was found. Reduction of DBSI-derived FA and of MTC at CEL onset also were strongly associated with PBH/PGH status at 12+ months. Non-significant relationships between increased DBSI-derived radial diffusivity and decreased DBSI-AD with later PBH/PGH status were also seen. Increased DTI-derived AD, but decreased DBSI-AD, were associated with subsequent PBH/PGH formation. We interpret these data to indicate that inflammatory edema occurring at time of CEL had confounded the interpretation of DTI-derived AD, as well as other DTI-derived parameters. Overall, DBSI has potential to differentiate anisotropic and isotropic components within imaged human white matter, and may yield insights into the evolution of MS lesion pathology.

Younce, John

Multifocal stroke with diffuse cerebral proliferation of small perforating arteries in the setting of cirrhosis with hepatopulmonary syndrome

Younce JR, Cross DT, Goyal MS, Lee JM

Abstract: Cirrhosis of the liver commonly causes systemic vascular changes including several changes to distal pulmonary arteries known as hepatopulmonary syndrome, characterized by microscopic intrapulmonary arteriovenous dilatations. Hepatopulmonary syndrome (HPS) leads to overperfusion relative to ventilation, ultimately resulting in ventilation-perfusion mismatch and hypoxemia. Similar changes in cerebral vasculature have not been described. We report the case of a patient with cirrhosis and HPS who initially presented with an intraparenchymal hemorrhage followed by months of stepwise cognitive decline. MRI brain demonstrated areas of diffusion restriction in bilateral medial occipital cortex and bilateral posterior corona radiata and centrum semiovale as well as small areas of susceptibility artifact on susceptibility-weighted imaging in the same regions, consistent with multifocal cerebral infarcts associated with microhemorrhages. Further investigation with cerebral angiography demonstrated generalized proliferation of small perforating arteries with diffuse arteriovenous shunting most prominent in regions with infarcts. While the etiology of these cerebrovascular phenomena are unclear, it is possible that infarcts may have resulted from shunting of oxygenated blood away from capillary beds, and hemorrhages may have resulted from local high flow states. The similarity of this patient's cerebral angiographic finding to the changes seen in HPS also suggests a similar etiology complicating hepatic cirrhosis.

Younce, John

Cortical atrophy correlates with adverse non-motor outcomes after STN DBS

Younce JR, Ushe M, Perlmutter JS, Norris SA

Abstract: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective treatment for Parkinson disease (PD) but is often limited by cognitive and other non-motor effects. We sought to investigate the relationship between cortical atrophy and non-motor clinical outcomes after STN DBS. We studied 92 people with PD that had DBS that had pre-op MRI structural imaging and preoperative and postoperative Unified Parkinson's Disease Rating Scale (UPDRS). Global cortical volume (CV) as well as volume of lateral parietal (LP), sensorimotor (SM) and perisylvian (PS) regions were compared to postoperative change in UPDRS1 (cognitive subscale) to investigate non-motor outcomes, and CV compared to postoperative change in UPDRS3 (motor subscale) to investigate motor outcomes. CV and LP volume individually correlated with UPDRS1; we found no other significant correlations. These results suggest a relationship between degree of cortical atrophy and adverse non-motor outcomes after DBS.