Washington University
School of Medicine
Department of Neurology

Residents' Day Symposium Friday,
May 29
7:15am – 9:15am

Platform/Poster presentations
will begin at 7:20am

Awards will be presented at 9:00am

We encourage everyone to attend this
important event.

Anderson, Christopher

Effects of procedural discomfort and expectation of benefit on therapy continuation in chronic migraine patients treated with onabotulinumtoxinA

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BACKGROUND: OnabotulinumtoxinA (Botox) has become a mainstream treatment for chronic migraine. Patients often have varied expectations for treatment success but little is known about how these initial impressions influence continuation of therapy.

OBJECTIVE: To record expectations of benefit and procedural discomfort from initial Botox treatment and to correlate with treatment success, defined as continuation of treatment for >3 sessions within a two-year period.

METHODS: A retrospective chart review of chronic migraine patients receiving initial treatment with Botox was performed. Patients were questioned about their expectations of benefit and procedural discomfort as rated on a 10-point scale. Adjusted and unadjusted logistic regressions were performed to determine odds of treatment success.

RESULTS: Responses from patients (N= 297) were analyzed. Unadjusted OR for expectation of benefit (p=0.087) and procedural discomfort (p=0.780) were not significantly predictive of continuing treatment. After adjusting for gender, age, and previous headache preventative trials, higher expectation of benefit (OR=1.134, p = 0.041) and female sex (OR=2.039, p=0.021) were found to be significantly predictive of treatment continuation.

CONCLUSIONS: Expectation of benefit and female sex may predict therapy continuation in patients initiating treatment of chronic migraine with Botox.

Atkas, Adam

Acute Disseminated Encephalomyelitis as a Paraneoplastic Manifestation of Epithelioid Hemangioendothelioma: A Case Report

Setting: Academic medical center

Patient: Young female with fever, hemiplegia, global aphasia, and bowel/bladder incontinence.

Case Description: A 23-year old female presented with the acute onset of right-sided hemiplegia, global aphasia, incontinence of urine and stool, and fevers. Head CT and brain MRI were concerning for left frontal lobe mass or infection with surrounding vasogenic edema. CT of the patient's chest, abdomen, and pelvis revealed multiple liver lesions.

Assessment/Results: Due to mental status decline and concern for herniation, the patient underwent a decompressive hemicraniectomy and brain biopsy. Left frontal lobe pathology was consistent with acute disseminated encephalomyelitis (ADEM) without evidence of infection or neoplasm. CSF cytology and flow cytometry was notable for marked acute inflammation without evidence of malignancy. Oligoclonal bands were absent. An autoimmune encephalopathy panel and paraneoplastic panel were negative.

Outside hospital records revealed that 10 months prior, the patient was admitted for emesis and diarrhea with an abdominal CT demonstrating multiple hepatic lesions. A liver biopsy demonstrated epitheliod hemangioendothelioma (EHE), a rare malignant vascular neoplasm. She was lost to follow up until her current presentation. She was admitted to acute inpatient rehabilitation and experienced a remarkable recovery of her aphasia and hemiplegia, functionally improving from requiring moderate assistance to complete independence.

Discussion: Despite the negative paraneoplastic panel, it was felt that the patient's ADEM represented paraneoplastic syndrome secondary to EHE. The paraneoplastic panel was negative as no specific antibody associated with paraneoplastic ADEM has been isolated. Thus, a negative paraneoplastic panel would not rule out paraneoplastic syndrome, but rather fail to identify paraneoplastic syndrome associated with the tested antibodies. ADEM presenting as a paraneoplastic syndrome has been reported in the literature, but never in association with EHE.

Conclusion: ADEM presented as a paraneoplastic syndrome secondary to EHE. Despite the patient's marked aphasia and hemiplegia on admission to inpatient rehabilitation, she made a remarkable recovery.

Butt, Omar

Very early network reorganization in cognitively-normal APOE ε4 carriers is related to tau not amyloid

Omar H. Butt, Julie K. Wisch, Suzanne Schindler, Anne Fagan, Tammie L.S. Benzinger, Carlos Chruchaga, John C. Morris, Beau. M. Ances
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Background: Apolipoprotein E (APOE) allele status is one of the strongest genetic risk factors for developing Alzheimer's disease (AD) (1-3). The ε4 allele has been linked to accelerated amyloid deposition (4) and neurofibrillary tau-tangle formation (5). Yet it remains unclear if the earliest cortical changes in cognitively normal APOE ε4 carriers is related to initial tau or amyloid seeding. In this study, we explore the relationship between very early cortical reorganization in asymptomatic individuals who have amyloid levels derived from cerebrospinal fluid (CSF) and positron emission tomography (PET) below established cutoffs for AD (biomarker-).

Methods: We obtained resting state functional connectivity (rs-fc) to evaluate changes in network integrity in a cohort of 121 cognitively intact (Clinical Dementia Rating [CDR] 0) participants (mean age 76.6 ±7.82 years, 15% APOE ε4 carriers, 65% female). All participants had both CSF and PET Pittsburgh compound B (PiB) evaluations that were below established cutoffs for AD (CSF Aβ42, CSF p-tau/Aβ42 and amyloid PET PiB-SUVR) (6). Rs-fc were aggregated into canonical cortical networks based on previously defined criteria (7). A 298x298 connectivity matrix was generated and masked to compare both intra-hemispheric (i.e. lateralized) and inter-hemispheric (i.e. callosal) connections between APOE ε4 carriers vs. non-carriers. Finally, linear modeling examined the relationship between network reorganization and biomarker levels, with subgroup analysis serving as validation.

Results: Early network reorganization in the default-mode (DM), memory (MEM), and salience (SAL) networks of APOE ε4 carriers was driven by changes in local, lateralized connections relative to long-

range callosal connections (rs-fc interaction term, p = 0.02; Fig A). Linear modeling (Fstat 2.68; p = 0.0074) of the rs-fc interaction term as a function of PET and CSF biomarkers revealed significant weighting for CSF p-tau (p = 0.03) and CSF t-tau (p = 0.03) but not CSF Aβ42 or PET-PiB (Fig B, with stepwise regression model Fig C). Results were identical for a subgroup (n = 74, 17% APOE ε4 carriers) for whom CSF t-tau/p-tau cutoffs were also included (rs-fc interaction term p = 0.02, linear model Fstat 3.51, p = 0.0014, with weighting for CSF p-tau and CSF t-tau but not CSF Aβ42 or PET-PiB).

Conclusions: Our findings suggest cognitively-normal APOE ε4 carriers have early network reorganization related to early tau formation that precedes significant amyloid deposition. This has important implications for both the timing and selection of therapies in primary prevention trials, with APOE ε4 carriers likely benefiting from anti-tau directed therapies that are administered very early, prior to significant amyloid or tau accumulation.

Chamessian, Alexander

Single Nucleus Transcriptomic Atlas of the Human Spinal Cord

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Background: The spinal cord requires a complex ensemble of neuronal and non-neuronal cell types to carry out its essential functions. Characterizing the full set of distinct cell types and their corresponding gene expression profiles is a necessary step toward understanding how these cells gives rise to the functioning of the spinal cord. Single cell transcriptomics studies in model organisms have revealed remarkable cellular heterogeneity of the spinal cord, but to date, there has not a comprehensive cellular atlas reported for human spinal cord. Thus, in this study, we aimed to fill this gap.

Methods: Flash-frozen post-mortem human spinal cord samples from the T12-L2 region were obtained from Anabios. Nuclei were isolated using Dounce homogenization and a standard nuclear homogenization buffer and then purified using fluorescence activated nuclear sorting (FANS) on a BD FACSAria II. Purified nuclei were then used as input to the 10x Chromium 3' Single Cell RNA-sequencing platform. Libraries were sequenced on the Novaseq 6000 (Illumina). Bioinformatics analysis included pre-processing with CellRanger, alignment and quantification with STAR, ambient RNA removal with CellBender, sample demultiplexing with souporcell. Downstream clustering, differential gene expression and visualization were performed in Seurat.

Results: After quality control, we obtained 17,911 high quality nuclei with at least 500 UMIs/nucleus and 250 genes/nucleus from 2 runs of the 10x Genomics platform, with median UMI of 10,810 and median gene count of 5226. Low resolution clustering and UMAP visualization of single nucleus transcriptomes resolved 24 separate clusters. Clusters were manually annotated using known marker genes for major cell classes. Non-neuronal cell types constituted the majority of cells, making up 98.3% of all cells; neurons constituted 1.7% of all cells. We identified 9 subtypes of Oligodendrocyte, 4 subtypes of Microglia, 3 subtypes of Astrocytes, 2 subtypes of Oligodendrocyte Progenitor Cells (OPCs), one subtype of endothelial cells and 2 putative immune cell types, most likely representing T-cells. Neurons clustered into a single group. Differential gene expression analysis revealed specific markers for each subtype, many of which have not been reported previously. Cell subtypes were compared to their

murine counterparts, and gene expression profiles were compared, with several species-specific differences apparent.

Conclusions: We report the first comprehensive single nucleus transcriptomic profile of the human spinal cord. Our dataset captured all known major classes of neural cell, and identified substantial heterogeneity within in cell type, consistent with single cell transcriptome results in brain. Based on stereological studies of human spinal cord, neurons are expected to constitute 10% of all cells. In our data, they only made up 1.7%, indicating a substantial loss of neurons, which may be due to technical and/or sample-specific factors. Future work will aim to determine the reason(s) for selective neuronal representation. We also aim to validate the cell types identified in this work using in situ methods, in both healthy tissue and diseased.

Chou, Chris

Comparison of single-channel EEG, actigraphy, and sleep diary in cognitively normal and mildly impaired older adults

Chris A. Chou, MD, Cristina D. Toedebusch, BS, Tiara Redrick, BA, David Freund, Jennifer S. McLeland, MA, John C. Morris, MD, David M. Holtzman, MD, and Brendan P. Lucey, MD MSCI.

Background: Sleep disturbances are hypothesized to be both an early marker of Alzheimer's disease (AD) pathology and a risk factor for development of AD. To further understand this two-way relationship, it is necessary to identify optimal devices for naturalistic sleep testing that minimize user burden and can be used on a large scale for screening and research. Polysomnography is the gold standard of measuring sleep but can be impractical for this purpose. Single-channel EEG (scEEG) and actigraphy are portable objective methods of assessing sleep that have been validated against PSG. Sleep diaries are used frequently in clinical sleep medicine and research. These three methods have yet to be directly compared to each in older adults with and without mild cognitive impairment.

Methods: This study is part of a larger ongoing observational study at the Knight Alzheimer's Disease Research Center at Washington University in St. Louis. 293 cognitively normal and mildly impaired participants were assessed by the Clinical Dementia Rating (CDR) and underwent up to six nights of at-home sleep testing with scEEG, actigraphy, and sleep diaries. Total sleep time (TST), sleep efficiency (SE), sleep onset latency (SOL), and wake after sleep onset (WASO) were calculated using each of these methods. 192 participants were cognitively normal (CDR 0) and 43 were mildly impaired (CDR 0.5).

Results: Of the four sleep parameters of interest, TST demonstrated the strongest correlations between instruments ($r = 0.466$-0.553, $p < 0.0001$). scEEG and actigraphy were found to have good clinical agreement with acceptably small mean differences for all sleep parameters. However, the correlation between scEEG and actigraphy worsened in mildly impaired participants. Sleep diaries were found to have clinically meaningful mean differences from scEEG and actigraphy in measuring TST and SE, but not SOL or WASO. Generally, correlations between diaries and scEEG or actigraphy were the weakest of all instrument correlations ($r < 0.4$, $p < 0.0001$ to 0.074), but did not differ with CDR status.

Conclusions: scEEG and actigraphy may be used interchangeably in cognitively normal older adults, but caution should be exercised when comparing between these methods in mildly impaired individuals. While sleep diaries may provide similar measurements for SOL and WASO to scEEG or actigraphy in older adults, they likely capture different aspects of TST and SE compared to objective instruments.

Cole, James

Central Cord Syndrome Resulting in Tetraplegia After Cervical Chiropractic Manipulation

James Cole, M.D., Sean Terada, MS3, Neringa Juknis, M.D.

Description: A 69 year old male with chronic neck and back pain and numbness presented to the emergency department after an episode of quadriparesis during a mechanical massage from a chiropractor. Patient was moving from his back to his side after a manipulation when he suddenly lost feeling in all four extremities but did not experience any acute pain. On presentation to the emergency department, he was at his baseline numbness in his upper extremities with loss of sensation and new weakness throughout upper and lower extremities bilaterally with increased tone in the upper extremities. He denied bowel or bladder incontinence, new neck or back pain, any loss of range of motion of neck, or changes in vision. Cervical spine MRI demonstrated degenerative disease with acute central cord compression and cord signal changes including edema from C3-6. Patient underwent decompression and fusion from C3-C6 and required short stay in ICU for blood pressure monitoring. Patient was subsequently admitted to inpatient rehabilitation, where he regained some strength but remained tetraplegic.

Discussion: Tetraplegia is a rare complication of chiropractic manipulation and current research is lacking on the need for evaluation of underlying pathology to assess patients at increased risk for adverse events. Underlying cervical spine pathology may increase risk for developing central cord syndrome from cervical manipulation but there are no current guidelines for determining patients who are poor candidates for this intervention.

Conclusion: While chiropractic manipulation is a generally safe intervention for patients with chronic neck and back pain, some patients may be at increased risk for developing spinal complications with lasting sensory and motor deficits even after surgery with decompression and fusion. Further research should be done to examine risk factors for spinal injury after chiropractic manipulation with possible development of standardized assessment prior to starting chiropractic manipulation.

Coman, Nick

Treatment of Autoimmune Glial Fibrillary Acidic Protein (GFAP) Astrocytopathy: A Case For Cyclophosphamide

Abstract:

Introduction: Autoimmune Glial Fibrilary Acidic Protein (GFAP) Astrocytopathy is a recently-characterized inflammatory disorder of the central nervous system which presents as a meningoencephalomyelitis — most commonly associated with encephalopathy and steroid-responsive MRI lesions of the subcortical white matter, diencephalon, and brainstem. While literature is limited at this time, it has typically been treated with IV steroids, IVIG, and plasmapheresis. Only one case employing Cyclophosphamide in treatment has previously been reported.

Case: A 35 year old male with a history of alcohol abuse presents with a subacute encephalopathy, opthalmoplegia, gait disturbance and is found to have GFAP astrocytopathy (+CSF antibody) after having previously been diagnosed with Wernicke's Encephalopathy. The patient did not initially respond to steroid or plasmapheresis treatment, but did show significant clinical and radiographic response after the induction of cyclophosphamide therapy.

Conclusion: This case evidences the potential utility of cyclophosphamide in cases treatment of GFAP astrocytopathy that have been refractory to steroids and plasmapheresis.

Fogarty, Alexandra

Differences in self-reported physical and behavioral health in musculoskeletal patients based on physician gender

Alexandra E. Fogarty, MD, Heidi Prather, D.O., Ryan Calfee, M.D. M.Sc., Graham Colditz, M.D., DrPH, MPH, Abby L. Cheng, M.D.

Abstract:

The association between patient health and the decision to request care from a physician of a particular gender is unclear. The purpose was to determine if there is a difference in self-reported PROMIS physical or behavioral health scores (Physical Function, Pain Interference, Depression, Anxiety) in patients who present to female (FP) versus male physicians (MP). This cross-sectional study analyzed 21,980 adult patients who presented to an orthopedic department of a tertiary academic medical center. Patients completed Patient-Reported Outcomes Measurement Information System (PROMIS) Computer Adaptive Test domains prior to the encounter: Physical Function, Pain Interference, Anxiety, and Depression. Primary outcome: the difference in mean PROMIS scores by physician gender. Secondary outcomes: differences in the proportion of patients meeting thresholds for clinically significant anxiety and depression; the proportion of patients reporting the floor (best) score for PROMIS Anxiety and Depression. Patients who chose to present to FP self-reported worse PROMIS scores for Physical Function (FP 40.2 ± 9.4, MP 42.4 ± 9.4,, $p < 0.001$), Pain Interference (FP 61.6 ± 7.6, MP 60.4 ± 7.7, $p < 0.001$), Anxiety (FP 52.5 ± 10.6, MP 51.4 ± 10.4, $p < 0.001$) and Depression (FP 47.5 ± 10.2, MP 46.2 ± 9.7, $p < 0.001$). Between-group mean differences did not meet MCID values, but the proportion of patients exceeding thresholds for heightened symptoms were: Anxiety: FP 741 (17.8%), MP 2,445 (15.1%), odds ratio 1.2 [1.1 to 1.3], $p < 0.001$; and Depression: FP 490 (11.8%), MP 1,426 (8.8%), odds ratio 1.4 [1.2 to 1.6], $p < 0.001$. Orthopedic patients who chose to present to female physicians instead of male physicians self-reported worse physical and behavioral health. Further investigation into this finding may provide insight into drivers of patients' preferences, which may enable physicians of both genders to provide the best care for their patients.

Garret, Mark

CSF Eosinophilia in Neuromyeltis Optica: A retrospective study of CSF findings in patients with AQP4+ NMO

Mark Garret, MD

Abstract:

Eosinophilic meningitis carries a narrow differential diagnosis including infectious, neoplastic, toxic, and inflammatory conditions but is not typically associated with demyelinating diseases such as neuromyelitis optica (NMO). Here we report an atypical case of a 32 year old woman with longitudinally extensive transverse myelitis associated with marked eosinophilic pleocytosis who was ultimately diagnosed with NMO. Retrospective chart review of AQP4+ NMO patients in the Washington University

Multiple Sclerosis clinic showed that 13/49 (26.5%) had detectable CSF eosinophils. Of these patients, 2/49 (4.1%) showed evidence of an eosinophilic meningitis with >10 eosinophils/cm3 and/or >10% eosinophils. Both of these patients had evidence of other systemic or CNS autoimmunity in addition to NMO, suggesting that their eosinophilia could be due to autoimmune overlap syndromes. Overall, these results suggest that NMO may be a rare cause of eosinophilic meningitis and should be considered in the differential diagnosis for this entity in the appropriate clinical context.

Gaudioso, Christina

Development of the Pediatric Quality of Life™ Multiple Sclerosis Module Items

Gaudioso, S Oo, VL Hendricks-Ferguson, P Newland, JW Varni, S Mar

Objective: Health-related quality of life (HRQOL) is conceived as one of the most pertinent measures in evaluating the effectiveness of clinical treatments. Currently, there is a deficit in disease-specific outcome measures to assess the HRQOL of children, adolescents, and young adults with multiple sclerosis (MS). The purpose of this study was to develop items and support the content validity for the Pediatric Quality of Life Inventory™ (PedsQL™) MS Module for children, adolescents, and young adults.

Methods: The iterative process included multiphase qualitative methods. A literature review of pediatric MS QOL was conducted to generate domains for focus interviews. An expert panel, comprised of twelve pediatric MS specialists, participated in the development of interview questions. Patients under 21 years of age and their parents then participated in semi-structured focus group interviews (n = 15), think-aloud-cognitive interviews (n = 15), and pilot testing (n = 10).

Results: Eighteen domains were derived from the qualitative methods. Once content saturation was achieved, 102 items were compiled. The domains composed included general fatigue, sleep/rest fatigue, tingling sensations, numbness sensations, physical weakness, pain, speech, balance, fine motor, vision, cognitive function, urination, constipation, bowel incontinence, anxiety, communication, treatment, and choice of medications.

Conclusions: Qualitative methods involving pediatric patients and their parents in the item development process support the content validity for the PedsQL™ MS Module. National validation and dissemination, using the large patient population from the US network of Pediatric MS centers, is forthcoming.

Hwang, Helen

A Single Molecule Assay for Detection and Characterization of Alpha-Synuclein Oligomers

Helen Hwang MD PhD, Melissa Stuchell-Brereton PhD, Andrea Soranno PhD, Paul Kotzbauer MD PhD

Abstract:

Parkinson's disease (PD) is a neurodegenerative disease characterized by loss of dopaminergic neurons in the substantia nigra. Alpha-synuclein accumulates as intracellular deposits in Lewy Bodies and Lewy neurites in the brains of affected PD patients. Levels of monomeric alpha-synuclein in CSF are significantly lower in PD patients than levels detected in control patients (Kang, JAMA Neuro. 2013,

Buddhala, Neurobiology Aging 2015). Currently, there is little known about the structure and concentration of oligomeric species in CSF, which are likely to be heterogeneous and difficult to detect.

We have developed and utilized a single-molecule pull-down spectroscopy assay to isolate and detect alpha-synuclein oligomers from CSF (Jain, Nature 2011). Using anti-alpha-synuclein antibody, we can selectively and specifically pull down oligomeric species isolated from recombinant alpha-synuclein fibrils. Surface-tethered antibody enables the capture of native protein complexes and their interacting partners for analysis at the single molecule level. Captured proteins can be visualized via fluorescently labeled antibodies, which allows us to analyze the number of alpha-synuclein monomers per oligomer by counting the steps visualized in photobleaching event counting assays. This new approach allows for single-molecule level quantification of the stoichiometry of oligomeric alpha-synuclein found in CSF or other biological samples from patients with Parkinson's disease.

Kang, Brian

Rehabilitation of Severe Functional Impairments Secondary to Autoimmune Glial Fibrillary Acidic Protein Astrocytopathy

Abstract:

Autoimmune Glial Fibrillary Acidic Protein (GFAP) astrocytopathy is a rare cause of eningoencephalomyelitis first identified in 2016. The pathogenesis leading to development of autoimmunity to GFAP is incompletely understood. Currently, no uniform diagnostic criteria exist for early identification of autoimmune GFAP astrocytopathy, which often leads to delayed diagnosis and/or treatment. Signs and symptoms can also be highly variable though fever, subacute headache, hyperkinetic movements such as ataxia or tremor, progressive cognitive deficits and confusion are reported with greater frequency in literature. This case describes a 35-year-old Asian male with a history of developmental delay and alcohol abuse who experienced a delay in immunosuppressive therapy after 9 weeks of visual hallucinations, confusion and increased lethargy which progressed to include ataxia, bradycardia and bowel and bladder incontinence. He presented to an outside hospital system 3 weeks after symptom onset. At that time, he was diagnosed with Wernick encephalopathy and discharged on oral thiamine. His cognitive function and ambulation declined rapidly after discharge in addition to experiencing new bladder and bowel incontinence. These symptoms led to his presentation at Barnes Jewish Hospital (BJH) 8 weeks after initial symptom onset. He was admitted and diagnosed with autoimmune GFAP astrocytopathy during his hospitalization at BJH and started on methylprednisolone and plasmapheresis 9 weeks after initial symptom onset. The patient was then discharged to inpatient rehabilitation to begin physical, occupational and speech therapies at 12 weeks after initial symptom onset where notable impairments included significant cardiopulmonary deconditioning and generalized weakness, dysphagia, flatness of affect with hypomimia, hypophonia, bradykinesia and impaired attention. He started cyclophosphamide monthly infusions during his rehabilitation stay and made only modest functional improvements at time of discharge. With earlier diagnosis and appropriate treatment, the patient may have made a greater functional recovery.

Kay, Benjamin

Setting Boundaries on the Effect of Motion on Resting State fMRI Inference

Benjamin Kay, MD, PhD, David Montez, PhD, Ryland Miller, PhD, Kristen Scheidter, BA, Scott Marek, BS, and Nico Dosenbach, MD, PhD

Abstract:

Head motion is the major source of artifact in MRI and functional MRI (fMRI) signals. Resting-state fMRI is a non-invasive brain imaging modality with great potential for investigating differences in neuronal connectivity related to Alzheimer's, epilepsy, autism, and other neurological disorders. However, the technical challenges posed by head motion cannot be understated. Small differences in head motion influence MRI signal in spurious but systematic ways. For example, early findings of decreased long-distance connectivity in Alzheimer's might actually have been due to higher motion in participants with advanced age and dementia. Numerous tools exist to mitigate head motion; we propose a novel method for measuring its residual effects on the specific hypothesis and variable under investigation. We demonstrate the feasibility of our method on resting-state fMRI data from 6,920 healthy children ages 9-10. Hypotheses regarding age, gender, intelligence, and personality are vulnerable to confounding by motion when its residual effects are not adequately accounted for.

Krill, Michael

An Atypical Source of Anterior Hip Pain in a 21-Year-Old Female

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Resident Physician in Physical Medicine & Rehabilitation, Department of Neurology, Division of Neurorehabilitation, Washington University in Saint Louis, Saint Louis, MO, 63108

A 21-year-old female was referred to the musculoskeletal physiatry clinic by her primary care physician for a 3-week history of progressive right hip and groin pain. She reported no trauma or clear precipitating mechanism of injury. However, about one month prior she noticed her right leg was longer than her left. Pain was worse with ambulation, prolonged sitting, or when lying directly on her right side. Her pain was tolerable when she was standing stationary or lying supine. She trialed short-courses of over-the-counter ibuprofen and topical menthol gel without improvement in symptoms. Her past medical history was notable for hypopituitarism, delayed puberty, and adrenal insufficiency. Her past surgical history included ligation of a patent ductus arteriosus and a left nephrectomy when she was extremely young with no known complications.

Physical examination was notable for tenderness to palpate on the right leg over the anterior superior iliac spine, anterior inferior iliac spine, and over the proximal rectus femoris. Passive range of motion of the right hip was limited in all directions due to end-range pain with hip flexion of 80 degrees, internal rotation of 15 degrees, and external rotation 30. Passive range of motion of the left hip demonstrate flexion to 95 degrees, internal rotation to 30 degrees, and external rotation to 40 degrees. Strength was 5/5 throughout all major muscle groups of the bilateral lower extremities with sensation intact to light touch throughout. She demonstrated an antalgic gait pattern on the right, but was able to heel walk, toe walk, and perform tandem gait without fall or loss of balance. Log roll test was negative bilaterally. FADIR, hip scour, and Stinchfield tests were positive only on the right, but FABER was positive and reproduced groin pain bilaterally.

Femoroacetabular impingement
Labral tear
Muscle/tendon strain
Stress fracture
Iliopsoas bursitis / internal snapping hip

Initial imaging included bilateral standing hip and Dunn view radiographs. Imaging demonstrated delayed-appearing complete closure of the growth plates of the femoral heads, worse on the right. There was abnormal lateral positioning of the femoral head epiphyses in relation to the femoral neck without evidence of acute injury. Brain MRI revealed an ectopic posterior pituitary gland with a hypoplastic anterior pituitary and nonvisualized pituitary stalk.

She was diagnosed with bilateral slipped capital femoral epiphysis. She was referred to endocrinology and diagnosed with panhypopituitarism, low estrogen, and vitamin D deficiency by endocrinology.

DISCUSSION – This unique case of slipped capital femoral epiphysis (SCFE) demonstrates the importance of maintaining a broad differential diagnosis and considering a patient's seemingly unrelated past medical history when creating that differential diagnosis. This patient's history of hypopituitarism and the intro articulate localization of the hip pain on physical examination led to the ordering of radiographs that ultimately led to the diagnosis of SCFE. SCFE can be classified as atypical or idiopathic. Traditionally, SCFE is a common cause of hip pain in adolescents usually between 8-15 years of age. Atypical SCFE, as seen in the patient above, is seen in cases associated with endocrine disorders, renal failure osteodystrophy, or radiation to the pelvis.

The patient was referred to orthopedic surgery where surgical intervention was recommended. She underwent in situ screw fixation for bilateral SCFE. Her post-operative radiographs demonstrated interval pinning of the bilateral femoral heads with mild residual slipped epiphysis, slightly greater on the right compared to the left.

The patient started out-patient physical therapy two weeks after surgery. At two- and ten-week follow-up she reported some residual anterior left hip pain. Initially, she demonstrated weakness mainly with hip external rotation, addiction, and abduction with the left leg weaker than the right. She was discharged from physical therapy at ten weeks with a home exercise program. At six months, she was able to return to work pain-free without assistive device.

Laws, Lindsay

Admitting Low-Risk Patients with Intracerebral Hemorrhage to a Neurological Step-Down Unit is Safe, Results in Shorter Length of Stay, and Reduces Intensive Care Utilization

Lindsay Laws, Flavia Lee, Rajat Dhar

Background and Purpose: Patients suffering intracerebral hemorrhage (ICH) are at risk for early neurologic deterioration and are often admitted to intensive care units (ICU) for observation. There is limited data on the safety of admitting low-risk patients with ICH to a monitored non-ICU setting. We hypothesized that admitting such patients to a neurologic step-down unit (SDU) is safe and less resource-intensive.

Methods: We performed a retrospective analysis of patients with primary ICH admitted to our SDU. We compared this cohort to a control group of ICH patients admitted to a neurologic-ICU (NICU) at a partner institution. We analyzed patients with supratentorial ICH ≤15cc, GCS≥13, NIHSS≤10, no to minimal IVH, and no other ICU indication. Primary endpoints were (re-)admission to a NICU and rates of hematoma expansion (HE). We also compared total NICU days and hospital length of stay (LOS).

Results: 80 patients with ICH were admitted to the SDU. Only two required transfer to the NICU for complications related to ICH, including 1 for HE. 74 SDU patients met inclusion criteria and were compared to 58 patients admitted to a NICU. There was no difference in rates of NICU (re-)admission (7 vs. 2, p=0.17) or rates of HE (3 vs. 5, p=0.28). Median NICU days were 0 vs. 1 (p<0.001). SDU admission was associated with shorter LOS (3 vs. 4 days, p=0.05).

Conclusions: Select patients with ICH can be safely admitted to a SDU. This may reduce length of stay and ICU utilization. Based on our and prior data, we propose criteria for admitting low-risk patients with ICH to a SDU.

Levasseur, Victoria

Gradient Echo Magnetic Resonance Imaging to Detect Central Vein Sign in Patients with Progressive and Relapsing Remitting Multiple Sclerosis

Victoria Levasseur, MD, Amber Salter, PhD, Biao Xiang, PhD, Dmitriy A. Yablonskiy, PhD, Anne H. Cross, MD

Abstract:

The diagnostic criteria for multiple sclerosis (MS) have undergone several iterations in the past 20 years resulting in increased sensitivity and earlier diagnosis, but also increased misdiagnoses due to reduced specificity. Biomarkers to distinguish MS from its mimics and to distinguish between MS subtypes are much needed. MS lesions in white matter typically form around a central vein, as shown by neuropathology. The central vein can be visualized with susceptibility-weighted imaging in all MS subtypes and can help differentiate MS from other diseases with white matter T2-weighted hyperintensities that look like MS lesions on standard MRI. It may also increase the sensitivity and specificity of MS diagnosis and simplify the diagnostic workup.

In this study, previously acquired MRI scans of progressive MS (n=25) and relapsing remitting MS subjects (RRMS, n=24) were analyzed for the presence of the CVS within identified lesions. The MRI based method gradient echo plural contrast imaging (GEPCI) was applied. Single reader detection of CVS, lesion volume, and anatomic location were recorded using publicly available imaging analysis software. The proportion of total lesions with CVS was calculated (CVS%) after excluding confluent lesions and lesions with more than 1 central vein. Differences in the median proportion between the progressive and RRMS subjects was evaluated using Wilcoxon sign rank test. Additionally, individual lesion CVS status was examined using generalized linear models to account for the within subject correlation of the lesions. Associations of CVS and clinical data acquired at the time of the MRI scan, including Expanded Disability Status Scale (EDSS), 25-foot timed walk, nine-hole peg test, paced auditory serial addition tests (PASAT), and symbol digit modality tests (SDMT) were made between the progressive and RRMS subjects using Spearman correlations. Our data show significant differences in disability, with the progressive group having higher EDSS scores and poorer performance on SDMT and MSFC. There was no significant difference in total CVS or percentage CVS per lesion between disease

subtypes. However, after controlling for EDSS and lesion volume, the RRMS group had a two-fold increased odds of having the CVS. Overall, it remains unclear whether or not the CVS is a useful measure to distinguish between MS subtypes. Additional analysis will include verifying if CVS is more common in specific anatomic locations, examining differences in proportion of CVS over total lesion volume for each subtype. We will also determine if lesions in progressive patients tend to have more than one central vein and if a higher proportion of CVS correlates with disability. Future studies will examine CVS in other demyelinating disease.

Mahdi, Jasia

Non-optic pathway tumors in children with Neurofibromatosis type 1 (NF1)

Jasia Mahdi, MD, Manu S. Goyal, MD, MSc, Jennifer Griffith, MD, PhD, Stephanie M. Morris, MD, and David H. Gutmann, MD, PhD

Objective: To define the radiologic features and natural history of non-optic pathway tumors (non-OPTs) in children with Neurofibromatosis type 1 (NF1).

Methods: We performed a retrospective cross-sectional analysis of 64 children with NF1 harboring 100 probable non-OPTs. Age at diagnosis, sex, tumor location, number of tumors, symptomology, concurrent OPT, radiographic progression (defined as qualitative and quantitative increases in size), and treatment were assessed. Tumor volumes were measured from initial presentation until treatment/end of disease progression.

Results: Sixty-three percent of probable non-OPTs progressed over time, where radiographic progression was concomitantly associated with clinical progression. Fifty-two percent of patients had incidentally-identified probable non-OPTs. Twenty-five percent of patients were symptomatic at initial diagnosis, all of whom harbored tumors that grew on subsequent scans and required tumor-directed therapy. There were no clinical differences between probable non-OPTs localized to the brainstem versus other locations with respect to age, sex, concurrent OPG, symptomology, and treatment. The average time from diagnosis to stabilization/decrease in tumor size was 2.34 years (SD = 2.15 years). Nineteen biopsied lesions were all histopathologically confirmed as tumor. Six children (9%) had deep extensive tumors, which presented earlier (mean age at diagnosis, 3.88 years), required multiple treatments, and had a shorter mean progression-free survival (48 months).

Conclusions: Over half of children with NF1 in this study developed probable non-OPTs, the majority of which were clinically and radiographically progressive. While brainstem and non-brainstem gliomas share similar clinical features and natural history, deep extensive tumors comprise a distinct aggressive group of tumors that warrant close attention.

Maher, Michael

Failed Back Surgery Syndrome in a 34 year-old-male

Michael E. Maher

Background: Post-Laminectomy Syndrome is defined as intractable pain, including chronic back pain and leg pain for which a spinal surgery has failed to produce improved, long-term clinical outcomes and

is present in ~30% of patient who have undergone surgery involving the discs of the lumbar spine. The rate of success of lumbar spine surgery is only marginally better than conventional medical management after 1 year and similar to medical management after 2 years. There are five categories of treatment: 1) Exercise, Physical Therapy, Behavioral Rehabilitation, 2) Medical management; 3) Interventional Procedures; 4) Neuromodulation and implantable technologies; 5) Reoperation. The strongest level of evidence is for active exercise, some interventional procedures, and spinal cord stimulator (SCS) implantation. SCS Implanation includes an insertion into the epidural space of electrodes connected to an external pulse generator that delivers electrical stimulation of large diameter afferents of dorsal column or dorsal roots and appears to inhibit nociceptive small diameter afferent transmission with median time to removal of 29 months.

Abstract: 34 year-old male with complicated-lumbago with post-laminectomy syndrome following two extensive lumbar spine surgeries in setting spinal stenosis and radiculopathy seen in the acute pain management clinic. Prior conservative treatment including physical therapy, medical management, interventional spine procedures, chiropractic treatment, and a TENS unit were noted to non-optimally improve pain. Functionally the patient ambulated with straight cane, had chronically poor sleep and was morbidly obese. The patient had recently went back to work and cared for a disabled child at home with the assistance of his wife. A pain psychologist who deemed the patient an appropriate candidate for SCS implantation next evaluated the patient and the trial was conducted.

Morris, Christian

A Stroke Syndrome

Morris, Christian

Abstract:

Setting: The Rehabilitation Institute of Saint Louis

57 y/o male pmh HLD who presents with dense right sided weakness, right-sided hemi-anopsia and right sided neglect and expressive aphasia. He was at a gas station in Huntsville Alabama and had a syncopal episode and lost consciousness. Subsequently taken to a hospital in Alabama where he underwent a HCT and CTA that showed an acute ischemic infarct in the left MCA distribution s/p thrombectomy and a possible small aneurysm in the ACA. The right-sided Hemi-anopsia subsequently resolved but the weakness, neglect and aphasia remained.

Rehab Hx: Lives with wife in a house; House has 2 stories, 2 stairs to enter and 14 stairs to 2nd floor; Employed as a salesman;

PLOF: Independent care, transfers, mobility; Highest level of education: College graduate

PE:

- Gen: NAD, sitting upright
- HEENT: EOMI, MMM, op clear
- CV: RRR
- Pulm: CTAB
- Abd: S/NT/ND +BS

- Ext: 2+ DP
- Skin: No rash
- Wounds: none appreciated
- Neuro:
- MS: AAOx4, attention appears normal, hard to assess memory given expressive aphasia.
- Expressive aphasia, with comprehension relatively intact, mixed up some commands with his left and right hand
- Follows simple commands. Mild Apraxia with hand movements
- CN: significant for central VII on right, right visual field cut, dysarthria.
    - There is intermittent disconjugate gaze but not reproducible.
- Reflexes: 2+ symmetrical, no clonus bilaterally
- FTN: no dysmetria
- Motor Strength:
    - 5/5 on left
    - 3-4/5 on right
- Decreased fine finger movements on right.
- Decreased sensation to light touch on the right UE
- Neuropsychological Evaluation Results: Gerstmann Syndrome, neuropsychological disorder characterized by a constellation of symptoms that suggests a lesion in the Supramarginal and/or Angular gyrus

Assessment: 57 y/o m pmh hyperlipidemia who presents with symptoms akin to Gerstmann Syndrome (Brain Imaging Unavailable at this time).

Plan:

- PT/OT/SLP
- Continent to bowel and bladder
- NDD4 Diet
- DVT ppx- Hep 5000 sq q8h
- HLD- Atorvastatin 40 mg qhs
    - Aspirin 325 mg qd

Park, Samuel

Hip radiograph findings in older adults undergoing image guided sacroiliac joint injections for posterior pelvic pain

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Introduction: Posterior pelvic pain in adults over the age of 40 can be attributed to lumbar spine, sacroiliac joint and hip disorders. Further, these disorders often co-exist. It is unknown what proportion

of older adults with the clinical symptom complex of sacroiliac joint (SIJ) pain have underlying hip deformity or hip osteoarthritis (OA).

Purpose: The purpose was to describe the prevalence of radiographic hip deformity and hip OA in a group of adults over the age of 40 who met the clinical diagnostic criteria for treatment of posterior pelvic pain with an image guided intra-articular SIJ injection.

Materials and Methods: Retrospective review identified 264 adults undergoing an SIJ injection for pain recommended and performed by 7 physiatrists practicing at a tertiary university orthopaedic department between 2011-2017. Hip radiographs were available in 248 adults and were read by a physician with expertise in hip measurements with previously demonstrated excellent intra-rater reliability. Percentages of hip deformity, hip OA and hip replacement (HR) are reported. Group differences of proportions by sex were assessed using Pearson chi-squared tests and Fisher's Exact test, as appropriate.

Results: Two hundred and forty-eight adults with mean age of 67.6 ± 10.9 years with 194/248 (78.2%) being female were evaluated. All had completed a trial of comprehensive non-invasive treatment for posterior pelvic pain and had a minimum of 3 positive SIJ provocative tests on physical examination.

Moderate to severe radiographic hip OA (Tonnis >2) was present in 27/248 (10.9%), and an additional 51/248 (20.6%) had previously undergone a HR. Of the patients with minimal to no OA and no history of HR, femoroacetabular impingement (FAI) pincer type was found in 66/170 (38.8%) and FAI Cam type was found in 17/132 (12.9%). Developmental hip dysplasia (DDH) was found in 30/170 (17.6%). Acetabular retroversion was found in 79/170 (46.5%) of adults.

There were no significant sex differences in the prevalence of moderate to severe hip OA, previous HR, or DDH, but a greater proportion of more men demonstrated Pincer (p=.032) and Cam (p=.047) FAI as well as acetabular retroversion (p=.011).

Conclusions: Approximately 1/3 of adults over the age of 40 with the clinical symptom complex of SIJ pain recalcitrant to non-invasive treatment were found to have moderate to severe hip OA or a previous HR. An additional 51.7% were found to FAI and 46.5% had acetabular retroversion. Men had a significantly greater prevalence of FAI and acetabular retroversion as compared to females. These radiographic bony hip deformities and arthritis may contribute to the clinical symptom complex of SIJ pain. Further study is needed in this age group of older adults to assess the links between hip OA, deformity and the pelvic girdle to better understand reasons for developing pain. This information would lead to alternative treatment options.

Perelstein, Elizabeth

A Proposed Methodology for Describing Neurology Inpatient Readmissions

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Objective: To establish a framework for examining a cohort of patients discharged from a neurology service and readmitted within 30 days.

Background: Readmission metrics are used as the basis for incentivizing and penalizing payment to hospitals. As a consequence, hospitals have focused on their readmission rates and attempted to reduce those numbers. However, to truly affect readmission measures requires improved accounting methods followed by description and root cause analysis of reasons behind readmissions. Methodologies for describing readmissions are not well-established. A standardized accounting framework would enable comparisons across hospitals, groups, and time.

Methods: Chart review was conducted on patients (1) hospitalized on a neurology/neurosurgery floor at a tertiary-care academic hospital, (2) discharged between January 1 2017 and June 30 2017, and (3) readmitted to the same hospital within 30 days of discharge.

Scheduled readmissions and neurosurgical readmissions were excluded from analysis. Of the remaining, unplanned neurology readmissions, two groups were delineated: preventable and non-preventable readmissions. Preventable readmissions were those which illness and process-related risk factors were identified, but not fully addressed during the initial admission. Non-preventable readmissions were defined as those admissions in which medical team oversight or process-related failures were not contributing factors to the readmission.

Of the non-preventable readmissions, three subgroups were defined: Disease Related-Predictable (RP), Disease Related-Unpredictable (RU), and Unrelated (UN). RP readmissions were defined as due to the development of common sequelae of the initial disease process. RU readmissions were defined as due to the development of uncommon sequelae of the initial disease process. UN readmissions were defined as due to factors completely unrelated to the initial admission.

Results: 130 readmissions were identified during the six-month study period. Applying the criteria described above, 59 neurology patients experienced unplanned neurology readmissions. Of these, eight were preventable readmissions, while 51 patients were readmitted from non-preventable factors. Further categorizing the non-preventable readmissions showed that 15% (9) met the RP criteria, 29% (17) the RU criteria, and 42% (25) the UN criteria.

Conclusion: The authors propose better defining 30-day neurology readmissions according to the above schema. Improving readmission descriptions would allow for better comparison across hospitals and time. This framework aims to separate readmissions related to predictable, modifiable risk factors from those without such factors. Distinguishing readmissions associated with easily-modifiable versus poorly-modifiable risk factors could be helpful in targeting resources to prevent early readmission.

Perez, Enmanuel

Interdisciplinary Initiative to Evaluate and Optimize Neurological Autoantibody Sendout Testing

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Abstract:

The last decade has witnessed a rapid expansion in the identification of antibody-associated and antibody-mediated neurologic disorders. While these advances have transformed the clinical practice of

neurology, they have also brought untoward consequences including excessive diagnostics and therapeutics driven by "false positive" results, inappropriate use of healthcare resources amidst "shotgun workups", and the added stress for neurologists in practice as they struggle to stay on top of this rapidly evolving field. To this effect, criteria, such as the APE2 and RITE2, have been developed by experts in the field to aid providers in their ordering practices. However, the performance and utility of these tools for guiding testing in clinical practice are yet to be independently validated. We prospectively utilized APE2 criteria along with expert review to advise providers on all autoimmune encephalopathy (AIE) and paraneoplastic (PN) panels ordered at Barnes-Jewish Hospital over a 3-month period (February to April of 2020). We then assessed the impact of this intervention on test volume and yield by comparing data to the three months prior to the implementation of the intervention. Amidst the Covid-19 pandemic and a reduced patient census, fewer tests were ordered during QI period. However, yield of testing (% positive) increased during the intervention period (for AIE 15% pre-QI vs 23% QI, and for PN 7% pre-QI vs 17% QI). The intervention correctly identified testing as indicated in all patients that ultimately ended up with positive results, while all tests pursued against recommendations of the intervention returned negative. Our preliminary results indicate a meaningful benefit from applying the APE2 scoring system in combination with expert review in guiding appropriate neurology specific autoantibody testing. We are now in the fourth month of our collaboration on this effort with colleagues in Laboratory Medicine with plans for continued investigation of the effects of this intervention on diagnostic yield, resource utilization, and patient centered outcomes.

Probst, Daniel

The Diagnosis and Treatment of an Isolated Axillary Nerve Injury in an Elite High School American Football Athlete

Daniel T. Probst MD, Susan E. Mackinnon MD, Heidi Prather DO

Setting: Academic medical center

Patient: High school football athlete with left deltoid weakness and atrophy.

Case description: The athlete tackled an opponent and experienced the immediate onset of numbness, tingling, and weakness throughout his left arm. He denied shoulder dislocation and his sensory symptoms improved. He finished the season with persistent left shoulder weakness. At presentation to our institution five months post-injury, physical exam revealed significant atrophy of the left deltoid muscle with decreased left shoulder abduction strength and decreased sensation over the left deltoid.

Assessment/Results: EMG demonstrated fibrillation potentials without motor units in the left anterior and middle deltoid heads consistent with complete denervation. In the posterior deltoid head, fibrillation potentials and motor units were present indicating denervation with some spontaneous reinnervation. The teres minor muscle was normal. A shoulder MRI confirmed subacute to chronic deltoid denervation and an unaffected teres minor muscle suggesting an isolated injury to a branch of the axillary nerve. The patient was urgently referred to a plastic surgeon with expertise in nerve injury (SEM). Approximately six months post-injury, the patient underwent a medial triceps nerve to axillary nerve transfer. After appropriate post-surgical therapy, the athlete returned to football the following season.

Discussion: Early identification and localization via EMG of peripheral nerve injuries in athletes is crucial. When performed within 3-6 months of a peripheral nerve injury, nerve transfers can lead to significant recovery. However, surgical outcomes diminish after a protracted time of injury, typically around 6 months. When diagnosed, our patient was 5 months post-injury with no visible voluntary motor units in 2 of the 3 heads of his left deltoid. The timing of his surgery likely contributed to his recovery.

Conclusion: An isolated injury to a branch of the axillary nerve was identified, localized via EMG, and successfully treated with a medial triceps nerve to axillary nerve transfer.

Ray, Christopher

Sensory ganglionopathy and ANNA-1 (Hu) seropositivity in a patient with Merkel cell carcinoma following exposure to pembrolizumab

Christopher Ray, MD; R. Brian Sommerville, MD; George Ansstas, MD; Robert Bucelli, MD PhD

Abstract:

Immune checkpoint inhibitors (ICIs) have revolutionized the treatment of many types of cancer, but are associated with a number of immune-related adverse events (irAEs). A patient with recurrent Merkel cell carcinoma (MCC) treated with a programmed death-1 (PD-1) inhibitor (pembrolizumab) developed profound sensory ataxia followed by gut hypomotility and encephalopathy. Electrodiagnostic testing showed evidence of a sensory ganglionopathy. The patient remained profoundly ataxic with progressive encephalopathy despite treatment with high-dose intravenous methylprednisolone and five rounds of plasmapheresis. Two additional cases with this triad of features (ANNA-1 antibodies in the setting of anti-PD-1 therapy for MCC) have been identified by colleagues at the Mayo clinic. As a neuroendocrine tumor, MCC has many features in common with small cell lung cancer (SCLC), the malignancy with the strongest association with ANNA-1 associated paraneoplastic disease. Our experience with this case has launched an interdisciplinary initiative to evaluate whether screening tumors for expression of neural antigens can be used to detect subjects at an increased risk of neurological irAEs following exposure to ICIs and other forms of cancer immunotherapy.

Sookochoff, Michael

An 18-Year-Old Field Hockey Player with Back and Leg Pain

History of Present Illness: An 18-year-old female field hockey player without significant past medical history presented for evaluation of one year of left-sided low back pain with radiation to the left buttock and posterior thigh. The pain was insidious in onset and there was no reported history of injury or trauma. The pain was sharp in quality with severity of 2/10 at baseline. The pain worsened to 8/10 approximately one hour after field hockey practices. It did not interfere with her ability to participate in field hockey. The pain was also acutely exacerbated by coughing and sneezing. It was associated with occasional numbness and tingling in the same distribution.

Exam: Her initial exam was significant for tenderness to palpation over the left L5-S1 junction, painful lumbar extension, and positive Gillet test on the left.

Tests and results: Radiographs demonstrated hemitransitional left L5 with pseudoarticulation with S1 and no instability on flexion/extension. MRI was obtained which redemonstrated transitional anatomy as well as central/left paracentral disc protrusion at L4-5 resulting in moderate central canal stenosis as well as possible abutment at the traversing left greater than right L5 nerve roots.

Working Diagnosis: Bertolotti Syndrome, L5 Radicular Pain, L4-5 paracentral disc protrusion with L5 abutment

Treatment and Follow-up: The patient was referred to physical therapy and advised to withhold from intense sporting activity until completion of physical therapy and then return to sport gradually, limiting activities that exacerbate symptoms. She returned to clinic approximately one year after her initial presentation. She reported improvement in symptoms though return of pain to previous baseline after discharge from PT. She had returned to sport and was able to play through pain.

Discussion: Lumbosacral transitional vertebrae (LSTV) are anatomical variants in which the L5 transverse processes (either unilateral or bilateral) are elongated and fused to a varying degree to the first sacral segment. These congenital variations are extremely common phenomena, likely with a prevalence between 5-30% of the general population. Approximately 13% of patients may develop symptoms, such as low back pain or tenderness and decreased lumbar or pelvic range of motion. Presence of pain in the setting of LSTV is known as Bertolotti Syndrome. LTSV may mimic sacroiliac, hip, or groin pain, and may even refer pain in an L5 radicular distribution ("pseudoradiculopathy"). Transitional vertebrae may also cause direct pressure on the exiting L5 nerve root resulting in compression radiculopathy. Our patient's symptoms were consistent with an L5 radicular pain pattern. Her physical exam was largely unremarkable. Given the presence of transitional anatomy as well as disc protrusion abutting the traversing L5 root at L4-5, her clinical picture was muddied. The exacerbation of her symptoms may be secondary to discogenic pain (coughing, sneezing, activity), though LVST may have similar presentation with low back pain and pseudoradiculopathy.

Conclusion: Lumbosacral transitional vertebrae are anatomical variations resulting in sacralization of the lowest lumbar vertebra. Symptoms associated with LSTV may mimic other more common causes of low back and radicular pain.

Triplett, Regina

Increased Maternal Inflammation during Pregnancy Affects Neonatal Brain Volumes at Birth

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Abstract:

There is a growing body of evidence linking maternal psychosocial stress to excessive immune activation during pregnancy and subsequently to adverse childhood neurodevelopmental outcomes. To further investigate the specific relationships between and critical windows of these influences, 390 mother-

infant dyads were recruited. Maternal serum concentrations of pro-inflammatory cytokines IL-6, IL-8, and TNF-□ and the anti-inflammatory cytokine IL-10 were collected during all trimesters of pregnancy and at delivery. Psychosocial measures at each trimester included maternal income-to-needs ratio as a measure of poverty and the Perceived Stress Scale (PSS). Infants underwent 3T brain MRI scanning within several days of birth. Automated segmentation of neonatal structural MRI data was performed, yielding standardized total volumes of cortical gray matter, white matter, and the cerebellum. Statistical analyses included only healthy infants born at ≥37 weeks EGA without prolonged neonatal hospitalizations. Concentrations of maternal IL-6 demonstrated the strongest relationships between income-to-needs ratios and PSS scores. IL-6 levels were higher among mothers with lower income-to-needs ratios, with the strongest relationship during the second trimester. IL-6 increased throughout the course of pregnancy with positive correlations across trimesters. Increased maternal IL-6 during the first trimester and at the time of delivery related to decreased neonatal total cortical gray matter volumes, after controlling for maternal income-to-needs ratios, PSS scores, and medical risk factors, and infant sex and OFC. These results support the effect of maternal inflammation on structural brain development in utero while highlighting the need for our forthcoming investigations of this cohort including detailed analyses of specific brain regions and the relationships with neurodevelopmental and behavioral outcomes during childhood.

Uzo-Okereke, Ada

FDG-PET hypometabolism changes after intracranial grid and strip placement

Uzo-Okereke MD, R. E. Hogan MD, M. Ponisio, MD, B. K. Day MD, PhD

Abstract:

We report the case of a 39-year-old man with refractory seizures who underwent an initial FDG-PET/CT study before intracranial electroencephalography (iEEG) was performed, using electrodes placed directly on the exposed surface of the left fronto-temporo-parietal convexity (64-contact subdural grid and strip electrodes). Initial intracranial video EEG monitoring did not adequately localize seizures, and the patient declined further workup for epilepsy surgery. After seizures remained refractory to medical treatment, he proceeded with re-evaluation for epilepsy surgery, which included a repeat FDG-PET/CT study. The second FDG-PET/CT study was obtained 79 months after iEEG.

The two PET time points were evaluated using both visual assessment, and the quantitative analysis tool (MIMneuro) for parametric mapping to calculate differences in tracer uptake in the patient's brain compared to a template of normal subjects (n =43). The results were fused with the most recently acquired brain MR for anatomical localization, and 3D brain cortical surface projections.

The parametric mapping analysis of the baseline FDG-PET/CT demonstrated markedly decreased metabolic activity in the left temporal lobe, without other significant abnormalities. The second FDG-PET, also processed using parametric mapping, showed a large region of greater than 2SD hypometabolism over the left fronto-temporo-parietal convexity. The hypometabolism was limited to superficial cortical regions. Coregistration of images with a volumetric CT of iEEG electrode placement showed that the left fronto-temporo-parietal region of hypometabolism correlated to the anatomic location of grid placement.

Our results document a chronic, incremental hypometabolic FDG-PET/CT change after intracranial subdural grid placement. The focal hypometabolic changes, confined to the region of intracranial grid

placement, are strongly suggestive of a causal relationship between grid placement and FDG hypometabolism. While definitive etiology of findings are uncertain, past neuroimaging studies documenting regional cortical edema after placement of iEEG electrodes, and past postoperative neuropathology studies documenting regional inflammatory changes in the region of iEEG placement are suggestive the iEEG could cause focal regions of cortical dysfunction. These findings are important for understanding brain functional changes after intracranial grid placement, and outline a potential avenue for comparison of intracranial strip and grid placement with other intracranial EEG techniques, such as stereotactic EEG with depth electrodes.

Wiltrout, Kimberly

Use of Whole Exome Sequencing in Epilepsy: A Case Series

Kimberly Wiltrout, MD and Judith Weisenberg, MD

Abstract:

Genetic etiologies are estimated to account for a significant proportion of epilepsy. However, there is no consensus on the best strategy for genetic testing in epilepsy. We describe four cases as evidence for the use of whole exome sequencing early in the course of epilepsy. Retrospective chart review was completed in four patients who were referred to the Epilepsy Center at Washington University/Saint Louis Children's Hospital. Whole exome sequencing (WES) was used to investigate the underlying genetic etiology of epilepsy in these patients. WES revealed pathogenic variants in genes that provide explanation for their epilepsy—LIAS, MOCS2, GAMT, and TUBB3. WES sequencing early in the clinical course can identify pathogenic variants providing an etiology for the patient's epilepsy. This can decrease the amount of additional evaluation patients must undergo as well as providing important prognostic information and potentially affecting management.

Wright-Jin, Elizabeth

Microglia sexual dimorphism in mice with heterozygous mutations in the Neurofibromatosis type 1 (NF1) gene

Wright-Jin, Elizabeth

Abstract:

Neurofibromatosis type 1 (NF1) is an autosomal dominant condition caused by germline heterozygous mutations in the NF1 gene on chromosome 17q11.2. While NF1 is completely penetrant, children with NF1 exhibit a wide array of clinical manifestations, with a significant degree of phenotypic variability. Several factors may underlie this clinical heterogeneity, including the specific NF1 gene mutation, genomic modifiers, environmental exposures, and sex. Sexually dimorphic phenotypes have been reported in children with NF1, including a higher rate of autism and optic glioma-induced vision loss in girls.

Prior studies in our laboratory have revealed both sex- and Nf1 mutation-dependent effects on microglia. To further study these effects in vivo, I quantitated microglia density in neonatal (P6-8) and young adult (6-8 weeks) male and female mice with or without heterozygous mutations in the Nf1 gene

(Nf1+/- vs WT) using Iba1 immunohistochemistry. I found that microglia density is unchanged in the neonatal hippocampus and in the young adult hippocampus, cerebellum, cortex, and brainstem. I also found no differences in microglia proliferation in the hippocampus of young adult mice. However, the density of microglia is significantly higher in the brainstem of neonatal females with Nf1 mutations. In summary, these results support the existence of sexually dimorphic phenotypes in the setting of NF1.

Yechoor, Nirupama

Racial Disparities of Ischemic Stroke in a Biracial Population

Nirupama Yechoor MD, MSc and Chia Ling Phuah MD, MMSc

Background: Previous literature investigating racial disparities in ischemic stroke has established higher rates of traditional risk factors and worse long-term functional recovery in African-Americans. However, these studies were limited by small proportions of black patients, and generalized stroke etiology. We present the first study to examine racial disparities in ischemic stroke by investigating differences in traditional risk factors, stroke etiology, and functional outcomes between African-American and Caucasian patients.

Methods: We performed a retrospective review of all MRI-proven strokes from August 2008 until March 2019 at the Washington University School of Medicine. Medical records were used to obtain demographics, medical history, inpatient stroke metrics, and 90 day functional outcomes. The primary outcomes were stroke etiology and 90-day modified Rankin Score (mRS).

Results: Of the 632 patients with MRI-proven strokes, 258 (40.8%) were black, and the median age was 58 (IQR 50-71) for black patients and 67 (IQR 54-76) for white patients ($p<0.0001$). The prevalence of Atrial Fibrillation was significantly less in black patients at 10% compared to 28% in white patients ($p<0.01$). Stroke etiology was also significantly different between white and black patients ($p<0.01$); small vessel disease is more prevalent in black patients, while cardioembolic and large vessel atherosclerosis account for the most common identifiable etiologies of stroke in white patients. Next, there was a significant difference in functional outcomes based on etiology of stroke by race; black patients with small vessel strokes had worse mRS scores when compared to white patients with the same etiology ($p<0.05$).

Discussion: Previously, it was hypothesized that higher rates of traditional risk factors and social determinants were responsible for worse outcomes after ischemic stroke in African Americans. We found that while black patients are younger, they also have higher prevalence of small vessel strokes. Moreover, compared to white patients, functional outcomes from small vessel strokes are worse in black patients. We hypothesize that this difference may be related to stroke location, and burden of existing white matter disease. Future studies could aim to investigate earlier primary prevention strategies, and possible genetic difference for stroke in African American patients.