Washington University
School of Medicine
Department of Neurology

Residents' Day Symposium

Monday, June 7, 2021
5:00pm – 7:00pm

Platform/Poster presentations will begin at 5:05pm

Awards will be presented at 6:45pm

We encourage everyone to attend this important event.

Brier, Matthew

Quantitative Signal Properties Derived from Routine Clinical Images Correlate with Clinical Disability in Multiple Sclerosis

Matthew R Brier, Abraham Z Snyder, Tammie LS Benzinger, Anne Cross, Robert T Naismith

Abstract:

Multiple sclerosis (MS) is an idiopathic demyelinating disorder of the central nervous system and is an important cause of neurological disability. MS is most commonly defined by clinical relapses which are associated with new, active demyelinating lesions detectable on routine magnetic resonance imaging (MRI). These white matter (WM) lesions provide diagnostic information and are used to monitoring disease activity or treatment efficacy. However, these lesions provide little prognostic information. Further, during the progressive stages of the disease, these lesions fail to track disease activity because progression of symptoms occurs absent discrete relapses. Thus, non-lesional measures of disease severity or progression are needed. Pathological abnormalities in normal appearing (NA-)WM and GM have been reported but extant imaging approaches require specialized sequences not available in large MS-imaging datasets or in clinical trials.

Here we develop a computational technique to extract quantitative measurements of tissue T1 and FLAIR (T2) which are informationally equivalent to measures derived from specialized sequences. We apply this technique to a large, observational cohort of patients with MS imaged with clinically available T1 and FLAIR sequences. In each individual, we extract measures of T1 and FLAIR signal intensity and variability in the NAWM and GM of MS patients.

We show that image signal intensity and variability measures reliably separate patients with MS from healthy controls. Further, relapsing-remitting patients are separated from patients with progressive MS; we found no distinction between the progressive disease subtypes. The non-lesional measures outperformed lesion based measures of disease severity for predicting functional impairment. When compared to atrophy based measures, the presently defined image intensity based measures provided complimentary information regarding MS-related disability. Finally, intensity abnormalities in the NAWM correlated closely with subcortical GM atrophy.

These results demonstrate that quantitative, informative non-lesional measures can be derived from clinical MRI data. Strong separation between controls and MS patients as well as relapsing vs. progressive disease suggests that non-lesional abnormalities are an important component of the disease process. Further, the predictive power of atrophy and non-lesional abnormalities compared to lesion-based measures strongly supports a view of MS wherein the lesion is the “tip of the iceberg” and abnormalities exist throughout normal appearing tissue. These biomarkers, applicable to existing clinical datasets, have the potential to be biomarkers of disease severity, monitor longitudinal changes, and assess response to therapy.

Chamessian, Alexander

Expression of Fibroblast Growth Factor Receptor 3 (FGFR3) in the Human Peripheral Nervous System: Implications for the Putative Role of FGFR3 Autoantibodies in Sensory-Predominant Idiopathic Neuropathy

Alexander Chamessian[1,2], Maria Payne[2], Diana Tavares-Ferreira[3], Theodore J. Price[3], Alan Pestronk[1], Robert W. Gereau[2]

1. Department of Neurology, Washington University School of Medicine
2. Department of Anesthesiology, Washington University School of Medicine
3. School of Behavioral and Brain Sciences, The University of Texas at Dallas

Background and Purpose: Autoantibodies to the Fibroblast Growth Factor Receptor 3 (FGFR3) have been associated with idiopathic sensory-predominant neuropathy characterized by painful paresthesias and non-length dependent distribution. The pathogenicity of FGFR3 autoantibodies in this disorder is unknown. Pathogenic mechanisms of autoantibodies in other dysimmune sensory neuropathies commonly involve direct binding of the autoantibodies to their cognate antigens on either neurons or glia. Therefore, as an initial step toward evaluating the pathogenicity of FGFR3 autoantibodies, we characterized the expression of FGFR3 in nerve, dorsal root ganglia (DRG) and spinal cord in human.

Methods: To characterize the expression of *FGFR3* mRNA, *in situ* hybridization (ISH, RNAscope) was performed on post-mortem fresh sections of human sciatic nerve, DRG and spinal cord. *FGFR3* transcript levels were also quantified by RNA-sequencing of nerve and DRG. Multiplex fluorescent RNAscope was performed on mouse DRG to compare to human. The expression of FGFR3 protein was evaluated using a high-sensitivity, automated capillary immunoassay (Wes, ProteinSimple) with multiple validated anti-FGFR3 antibodies.

Results: *FGFR3* mRNA was not detected in nerve or DRG but was abundant in SC by RNAscope. Consistently, RNA-seq demonstrated very low transcript counts for *FGFR3* in nerve and DRG. FGFR3 protein was absent from nerve and DRG by capillary immunoassay but was moderately expressed in the spinal cord.

Conclusions: A direct pathogenic mechanism of FGFR3 autoantibodies in sensory neuropathy would require the expression of FGFR3 in either neurons or non-neuronal cells in the nerve or DRG. Using multiple methods, we did not detect FGFR3 expression at the mRNA or protein levels in nerve or DRG. Consistent with prior studies, we did detect FGFR3 mRNA and protein in the spinal cord, where it is known to be expressed by astrocytes. Given the absence of FGFR3 from nerve and DRG, it is improbable that FGFR3 autoantibodies cause direct damage to the neural structures involved in neuropathy.

Crockett, Cameron

Variability in diagnostic yield of exome sequencing by clinical phenotype: Review of 1053 cases from a single center

Cameron D. Crockett MD, Laura Jansen MD PhD, Tychele Turner PhD, Brian Leon-Ricardo MS, Marwan Shinawi MD, Dustin Baldridge MD PhD, Christina Gurnett MD PhD

OBJECTIVE: Exome sequencing (ES) has become an important element of the evaluation of many patients with undiagnosed neurologic diseases. We report our institutional experience regarding diagnostic yield in relation to neurologic phenotypes.

METHODS: Retrospective review of clinical data collected on patients who underwent clinical ES between May 2015 and January 2020 at the Washington University Undiagnosed Mendelian Disorders Exome Clinic and who were consented for research analysis of ES and clinical data. ES data was generated as part of routine clinical care by GeneDx and other diagnostic laboratories. Patients were referred primarily by clinical geneticists, child psychiatrists, and pediatric neurologists.

RESULTS: A total of 1053 patients were included, 55.8% of which were male. Average age was 11 years, with a range of 0-83 years. Of the full cohort, 256 (24.3%) had genetic variants reported as having a definitive relationship to phenotype and were considered “solved” for purposes of this study. Fine and gross motor delays as well as intellectual disability were historical findings associated with higher solve rates. Hypotonia and presence of facial dysmorphisms were examination features associated with higher solve rates. Cerebral atrophy was the only structural brain abnormality associated with increased solve rate.

CONCLUSIONS: ES is a useful tool for the evaluation of patients with a variety of clinical phenotypes of unclear etiology. This study suggests that variable diagnostic yield may be expected based on clinical phenotype. Further investigation into these variances may allow for more cost-effective approaches to testing based on an individual patient’s phenotype.

Dixon, Sarah

Implementing an Advocacy Curriculum for Child Neurology Residents

BACKGROUND: Competency in systems-based practice and advocacy are increasingly recognized as necessary milestones for residents, but relatively little time is dedicated to advocacy training during residency. We sought to understand perceptions of advocacy training and whether implementing a curriculum affects perceived ability to be an effective physician advocate.

METHODS: An electronic survey was distributed to faculty and trainees in the Department of Pediatric Neurology at Washington University in St. Louis in the winter of 2020 to evaluate baseline perceptions about advocacy training. Survey results were used to create a curriculum comprised of a lecture series with an experiential learning component, the "Spring into Action Advocacy Challenge." A follow-up survey was distributed to assess perceived value and change in abilities.

RESULTS: Pre-curriculum survey response rate was 77% (n=27) for faculty and 76% (n=13) for residents/fellows and post-curriculum response rate was 20% (n=7) for faculty and 23% (n=4) for residents/fellows. Most respondents (65%) had little to no prior training related to advocacy. The most commonly identified barriers to participating in advocacy were time (24%) and lack of skills required for advocacy (18%). From the pre-curriculum survey, 75% saw need for a curriculum and 100% identified this need on the post-survey. The majority of respondents felt slightly to moderately confident in their ability to participate in advocacy as physicians (68% on pre-survey and 90% on post-survey).

CONCLUSIONS: Implementation of an advocacy curriculum was highly valued within our child neurology residency training program. Curricula should address commonly identified barriers to participating in advocacy. Further understanding is needed about how to best evaluate advocacy curricular outcomes and which activities improve competency.

Dukes, Brittany

Evolving Shoulder Pain: A case report

Andrew O'Halloran, MD, Brittany Dukes, MD, Michael Krill, MD

Case Diagnosis: 62-year-old female with one-year of evolving right shoulder pain

Case Description:
Relevant history included right carpal tunnel syndrome and remote proximal humerus fracture complicated by non-union managed with ORIF 13 years ago with subsequent revision 2 years following. She first noticed lateral shoulder pain 10 months ago after lifting office supplies overhead, worse with movement and side laying. An outside physician initially provided a glenohumeral steroid injection without improvement. She was then seen by Orthopedic surgery two months later, who provided a subacromial bursa injection, physical therapy referral, and ordered a diagnostic ultrasound (US). US revealed full-thickness right rotator cuff tear involving the posterior supraspinatus and infraspinatus tendons and normal biceps tendon. Patient returned several weeks later with medial elbow pain and paresthesias consistent with medial epicondylitis with ulnar neuritis. She was subsequently provided new PT prescription, NSAIDs, and brace. Patient returned two months later, with predominantly anterior shoulder pain concerning for biceps tendonitis and was referred to PM&R for US injection of right bicep tendon sheath. US revealed the screw was in direct contact with the long head of biceps tendon (LHB).

Discussion:
This case highlights the dynamic nature of musculoskeletal care as well as the importance of personally reviewing diagnostic imaging.

Setting:
Outpatient musculoskeletal clinic

Assessment/Results:
Patient was tender to palpation via US probe over area of the bicipital groove. US revealed the anterior projecting humeral screw was in direct contact with the LHB. Procedure was converted from corticosteroid injection to complete diagnostic US evaluation. Review of remote X-rays of humerus demonstrated a screw projecting anterior to the humeral cortex. Findings were discussed with the referring surgeon and patient subsequently underwent right arthroscopic rotator cuff repair, bicep tenotomy, and subacromial decompression, currently progressing well postoperatively.

Conclusion:
A thorough evaluation should be performed before moving forward with corticosteroid injections. In the event of new or unexpected findings, clinicians should adjust plan accordingly.

Fogarty, Alexandra

The Living Well Center: A pilot study of a lifestyle medicine program in patients with musculoskeletal disorders

Objectives

Lifestyle medicine utilizes a multidisciplinary approach to manage both medical and psychosocial barriers to wellness. The primary aim of this study was to access the feasibility of this approach to care in patients presenting with musculoskeletal disorders. The secondary aim included characterization of patient goals, program usage, and symptomatic improvement.

Design

Patients were referred from the orthopedic department of a tertiary care academic medical center for consultation with a lifestyle medicine program physician. Treatment goals, demographics, and physical and behavioral health Patient-Reported Outcomes Measurement Information System (PROMIS) measures were collected at baseline and re-assessed at discharge. Descriptive analysis was performed regarding patients' treatment goals, program usage, and symptom changes.

Results

26 patients with a mean age of 58 years (range 21-78 years) were enrolled in the program between 11/2018 and 6/2020 . Nineteen were enrolled with a primary spine diagnosis (lumbosacral radiculopathy (n=12), lumbar spondylosis (n=4), lumbar spinal stenosis (n=1), and/or myofascial back pain=2), and 10 were enrolled with symptomatic osteoarthritis (knee (n=6), hip (n=3), and tarsometatarsal (n=1)). At analysis, 19/26 patients had discharged. The average number of total visits was 8.2 (95% CI 6.6 – 9.7; SD 2.4, range 0-6;), over an average of 115 days (95% CI 86 - 145). In addition to their visits with the program physiatrist, patients worked with other professionals with an average of 2.8 visits overall (SD 3.6, range 2-6). A total of 89% (17/19) of patients worked with the psychologist, 94% (18/19) received acupuncture, 89% (17/19) participated in nutrition counseling, 73% (14/19) received massage therapy, and 86% (16/19) engaged in physical therapy. There was a statistically significant reduction of PROMIS Anxiety score (-4 points; p=0.05) (see table).

Conclusion

This pilot study demonstrated overall feasibility of a lifestyle medicine program for musculoskeletal disorders. On average, physical function and anxiety symptoms improved by a clinically meaningful degree, and nearly half of discharged patients met their goal. Refinement of patient selection may further optimize the success rate of such a program.

Galardi, Maria Milagros

Posterior reversible encephalopathy syndrome: are children more likely to present "atypically"?

Maria Milagros Galardi, Cori Grant, Amir Orandi, Kevin Barton, Vivek Pandey, Andrew White, Ali Mian, Shannon Agner

Objectives:

1. To establish the incidence of seizure at onset and subsequent seizures in pediatric PRES and investigate the use of anti-seizure medications (ASMs) in this population
2. To determine the prevalence of "atypical" radiologic features in pediatric PRES cases
3. To determine the prevalence of persistent radiologic findings in pediatric patients with PRES

Methods:

Probable and confirmed cases of PRES seen from 2000-2018 in a tertiary care children's hospital were identified from electronic medical records and retrospectively reviewed.

Results:

Forty-one cases of pediatric PRES were included in the study. Mean age at presentation was 12.46 years. 65.9% were female. 65.9% were white and 31.7% were black. All patients had a primary diagnosis in one of the following categories: organ transplant (29.3%), autoimmune/inflammatory disease (24.4%), renal disease (19.5%), bone marrow transplant (14.6%), and infection (7.3%). Thirty-two patients (78%) had seizures as part of their initial presentation, 11 (26.8%) of which presented with status epilepticus. Maintenance anti-seizure therapy was initiated in 19 (59.4 %) of the patients presenting with seizures. Five patients with seizures that were on ASMs at time of presentation had doses increased. On initial brain magnetic resonance imaging (MRI), 41.6% had diffusion restriction and 19.5% had hemorrhage. 19 patients had follow-up MRI's, 15 of which showed complete resolution of edema. Structural sequelae were identified in follow-up MRI's for 10 patients including gliosis, atrophy, and/or laminar necrosis. Four patients had recurrence of seizures within 1 month of initial presentation. One patient went on to develop unprovoked seizures 18 months after diagnosis of PRES

Conclusion:

In this retrospective study of pediatric patients with PRES, the majority had seizures as part of their presentation. Status epilepticus may be more prevalent in pediatric PRES patients than adult patients with PRES. Diffusion restriction on MRI might be more prevalent in children than adults with PRES.

Gaudioso, Cristina

Analysis of MOG and Aquaporin-4 Antibody Frequency among Children Diagnosed with MS and Controls: A comparison of seropositive and seronegative cases.

Cristina M Gaudioso[1], Eoin P. Flanagan[2], Adam Nguyen[2], Charles T Casper[3], Rachel Codden[3], Gregory Aaen[4], Anita Belman[5], Leslie Benson[6], Meghan Candee[7], Tanuja Chitnis[8], Mark Gorman[6], Manu Goyal[1], Jennifer Graves[9], Benjamin Greenberg[10], Yolanda Wheeler[11], Ilana Kahn[12], Lauren Krupp[13], Timothy Lotze[14], Jayne Ness[11], Mary Rensel[15], Moses Rodriguez[16], John Rose[17], Jennifer Rubin[18], Teri Schreiner[19], Jan-Mendelt Tillema[16], Amy Waldman[20], Bianca Weinstock-Guttman[21], Jessica Sagen[2], Emmanuelle Waubant[22], and Soe Mar[1]

Background: Myelin oligodendrocyte glycoprotein (MOG)-IgG associated disorder (MOGAD) and aquaporin-4-IgG (AQP4-IgG) positive neuromyelitis optica spectrum disorder (AQP4-NMOSD) are distinct diseases from multiple sclerosis (MS) and all three are recognized to occur in children. There is a paucity of data on the frequency of MOG-IgG and AQP4-IgG among patients diagnosed with pediatric-onset MS (POMS) in the USA and these antibody biomarkers have not been studied in pediatric healthy controls. Using a well-defined, prospectively characterized cohort of children with a prior working diagnosis of MS and healthy pediatric controls, we aimed to (1) determine the frequency of MOG-IgG and AQP4-IgG in both groups; (2) compare demographics, clinical, biological and MRI characteristics, disease course and outcome in seronegative children with MS versus seropositive children with MOGAD or AQP4-NMOSD; (3) identify predictors of final diagnosis.

Methods: POMS and frequency matched controls were enrolled from November 1st, 2011 to July 1st, 2016 at 14 sites in the USA as part of a case-control study on risk factors for POMS. Follow-up data on the POMS group was prospectively collected and entered in a web-based registry as part of a national network. AQP4-IgG and MOG-IgG were assessed on sera available from pediatric cases and controls using a live-cell based assay technique at the Mayo Clinic neuroimmunology laboratory (Rochester, MN). Demographics, clinical, biological and MRI characteristics and disease course were recorded and then compared between seropositive and seronegative cases.

Findings: We included 1196 participants, 493 with a prior working diagnosis of MS and 703 healthy pediatric controls. AQP4-IgG was negative in all cases and healthy controls. MOG-IgG was positive in 30 of 493 cases (6%) and negative in all healthy controls. MOG-IgG seropositive cases were assigned a final diagnosis of MOGAD while seronegative cases were given a final diagnosis of MS. MOGAD cases, when compared to MS, were more commonly female (25/30 [83%] vs. 297/463 [64%]; p=0.032), presented at a younger age (mean 9.1±4.7 vs. 14.7±2.6 years; p<0.001), had presenting symptoms more commonly localized to the optic nerve (20/30 [69%] vs. 125/463 [32%]; p<0.001) and less commonly to the spinal cord (5/20 [22%] vs. 192/463 [51%]; p=0.007), were more likely to present with an ADEM-like phenotype (8/30 [27%] vs. 9/463 [2%]; p<0.001), and were less likely to have serum Epstein-Barr virus positivity (14/30 [47%] vs. 442/463 [95%]; p<0.001) and cerebrospinal fluid oligoclonal bands (10/30 [33%] vs. 238/463 [51%]; p=0.055).

Interpretation: MOG-IgG and AQP4-IgG were not identified among a large number of pediatric healthy controls confirming the high specificity of these antibody biomarkers for CNS demyelinating disease in children. A small proportion of those with a prior working diagnosis of POMS ultimately had MOGAD but none had AQP4-NMOSD. Predictors of a MOGAD diagnosis versus MS included female sex, younger age at disease onset, first demyelinating disease diagnosis of ADEM-like phenotype, and presenting symptoms localized to the optic nerve. While it is possible that POMS can have false positive MOG-IgG, it is very rare.

Harrison, Mysti

Central Vein Sign in Pediatric Multiple Sclerosis and MOG Antibody Associated Disease

Kimystian Harrison, MD, MS[1]; Cristina Gaudioso, MD[1]; S. Richard Dunham, MD[1]; Victoria Levasseur, MD[1]; Natalie Schanzer, BA[1]; Amber Salter, PhD[2]; Manu Goyal, MD[3]; Soe Mar, MD[1]

Affiliations: [1]Washington University in St. Louis School of Medicine, Department of Neurology, St. Louis, MO, USA; [2]Washington University in St. Louis School of Medicine, Department of Biostatistics, St. Louis, MO, USA; [3]Washington University in St. Louis School of Medicine, Department of Radiology, St. Louis, MO, USA

Background: Multiple sclerosis (MS) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) are demyelinating conditions of the central nervous system that have been difficult to distinguish based on clinical presentation or MRI findings. MOG-IgG titers are used to help differentiate between MS and MOGAD currently, but have been unreliable as MOG-IgG titers fluctuate, titer thresholds are not yet clear, and titers can become undetectable between relapses. MOGAD is detected in up to 30% of children with acute demyelination and treatment options and prognosis are different for MOGAD and MS. Thus, early and accurate diagnosis is essential. The central vein sign (CVS) on brain magnetic resonance imaging (MRI) is now a promising marker for adult MS and can differentiate MS from its mimics. The presence of this marker is not well established in pediatric patients.

Objectives: We aimed to evaluate the rate of CVS within demyelinating lesions of the brain in children with MS and MOGAD and determine its diagnostic value in distinguishing these diseases.

Methods: Patients with a diagnosis of pediatric onset MS (POMS) or MOGAD at last follow-up were identified in a pediatric demyelinating database at St. Louis Children's Hospital, which was maintained for the US Network of Pediatric MS Centers. Two reviewers, blinded to the clinical diagnosis, retrospectively reviewed clinically obtained brain MRIs in each of these patients. Fluid attenuated inversion recovery (FLAIR) sequences were used to identify lesions. Susceptibility weighted imaging (SWI) fused to the FLAIR sequences were used to assess the prevalence of CVS. Differences in CVS between POMS and MOGAD were evaluated, and agreement in CVS number was reported using an intraclass correlation coefficient (ICC).

Results: A total of 20 pediatric patients, 10 with POMS and 10 MOGAD, were assessed. Mean (SD) age was 11.6(4.7) years in POMS and 7.1(3.3) years in MOGAD. 60% in POMS and 70% in MOGAD were female. The CVS was significantly more prevalent in POMS when compared to MOGAD, 53% of total lesions compared to 19%, respectively ($p<0.001$). Inter-rater reliability for identifying the total number of white matter lesions was good (ICC 0.94 [95%CI: 0.84, 0.97]). However, the inter-rater reliability for detecting the number of CVS lesions was poor (ICC -0.17 [95%CI: -0.37, 0.58]).

Conclusion: The CVS can be a useful diagnostic tool to help differentiate MS from MOGAD in pediatric patients, but poor inter-rater reliability using current clinical brain MRIs may limit the usefulness of CVS in individual cases. Application of CVS to individual cases of MS versus MOGAD could be improved with an MRI sequence optimized for detection of CVS, as well as a validated automated assessment to diminish the effects of variability between reviewers.

Harrison, Nigel

Late onset dopa responsive oromandibular dystonia in FXTAS

Abstract:

Here we report a case of oromandibular dystonia that was responsive to dopamine therapy in the setting of fragile X tremor ataxia syndrome (FXTAS). This case adds to the diverse presentation of FXTAS.

Heuermann, Robert "BJ"

Effects of dopamine on pain-responsive neurons in the central amygdala

Abstract:

Pain is one of the most common nonmotor symptoms in Parkinson disease (PD), reported by up to 80% of patients, but often goes under-recognized and under-treated. In addition to musculoskeletal sources of pain due to dystonia and abnormal posture, there is evidence of aberrant central pain processing in both human studies and animal models of PD. While the mechanisms behind this central sensitization remain largely unexplored, we hypothesize that dopamine normally suppresses central pain networks, and thus loss of dopamine in PD leads to pain hypersensitivity. We used the TRAP mouse line (Transient Recombination in Activated Populations) to fluorescently label neurons activated by a painful stimulus, for subsequent targeting for ex-vivo patch-clamp recordings. In neurons of the central amygdala (CeA), an important node for pain processing, application of dopamine reduced cell excitability and the strength of synaptic inputs, consistent with our hypothesis. Future experiments will use optogenetic techniques to manipulate dopamine signaling in the CeA in awake behaving mice, to test whether this affects pain thresholds and nocifensive behaviors.

Holloman, Jameson "Jamie"

Exploring the role of the ion channel TRPV4 in the pathogenesis of Multiple Sclerosis

Abstract:

TRPV4 is a non-selective Ca2+ permeable channel expressed on a variety of cells, including neurons, microglia and peripheral macrophage. TRPV4 has been implicated in peripheral neurologic dysfunction associated with itch, pain and neuropathy. TRPV4 inhibition has been found to reduce microglial activation and decrease neuroinflammation whereas activation of TRPV4 has been shown to induce macrophage phagocytosis and cytokine production in mice. TRPV4 inhibition has also been found to improve myelination and reduce glial reactivity in the cuprizone mouse model of MS. This data, in conjunction with preliminary obtained by the Wu lab, indicates that TRPV4 plays a role in the pathogenesis of MS and could serve as a potential therapeutic target. My experiment explores the role of TRPV4 in microglial and peripheral macrophage activity to discern it's possible role in the pathogenesis of MS. We hypothesize that TRPV4 activation induces a pro-inflammatory response from microglia and macrophages and propagates neuroinflammation and neurodegeneration in MS. We used calcium imaging of human peripheral monocytes, TRPV4 knockout mouse models of EAE and Cuprizone, and microglia cultures to test this hypothesis.

Kang, Brian

Cauda Equina Syndrome in the setting of Neurosarcoidosis: A Case Report

Brian Kang PGY-3, Michael Krill PGY-4, Neringa Juknis

Abstract:

Neurosarcoidosis is a manifestation of sarcoidosis involving the CNS appearing in approximately 25% of patients diagnosed with sarcoidosis, 1-18% of this population involve the spinal cord and within this population, only a handful of cases have been reported that involve the cauda equina and/or the conus medullaris. Thus, cauda equina syndrome secondary to neurosarcoidosis represents an exceedingly rare diagnosis without established guidelines for the management of patients with this condition. The current standard of care involves variable taper of corticosteroids with or without long-term immunosuppression. Here we describe a case of a 43-year-old female with history of ulcerative colitis who developed new-onset constipation that progressed to worsening low back pain, urinary incontinence, saddle anesthesia and lower extremity (LE) weakness. Examination was notable for patchy loss of sensation in bilateral LEs originating at T11, accompanied by weakness (3-4/5) throughout bilateral LEs with hyporeflexia. She received high dose steroids with improvement in symptoms and was discharged to acute inpatient rehabilitation (IPR) for further therapy, including neurogenic bladder care and training. Patient progressed at IPR and was independent or modified independent for all activities of daily living (ADLs) when discharged after which she developed new neuropathic pain with occasional urinary retention at 6 months that was treated with addition of methotrexate. Neurosarcoidosis diagnosis was confirmed by imaging, clinical improvement with prednisone and methotrexate and negative infectious work up. Cauda equina syndrome is a very rare manifestation of neurosarcoidosis with less than 25 cases reported. The exact role of IPR is not established, but given the severity of this condition, patients may benefit to assist with activity modifications for ADLs.

Kapadia, Jeet

Case of Pembrolizumab causing PML-IRIS

Abstract:

This is a case presentation on a patient who had metastatic breast cancer. Due to wide spread metastasis she underwent pembrolizumab treatment for this disease. Shortly after treatment the patient started to develop symptoms of slurred speech, ataxia which was progressive for 1-2 months and left the patient non ambulatory. The patient was found to have inflammation in the cerebellum and found to have JC virus positive in the CSF. The thought is after starting pembrolizumab it caused the immune system to attack the JC virus and therefore causing worsening symptoms.

Katzen, Seth

An Atypical Cause of Hip Pain in a Young Adult Female: A Case Report

Seth M. Katzen, DO; Michael Krill, MD; Daniel Probst, MD; Jeremy Hartman, MD
(Washington University in St. Louis School of Medicine/
Barnes-Jewish Hospital, Saint Louis, MO)

Disclosure: None

Setting: Tertiary Care Academic Hospital

Patient: A 21-year-old female with 3 weeks progressive right hip and groin pain

Case Description: The patient reported no clear mechanism of injury but did notice a clear R>L leg length discrepancy which had developed in the presenting time frame. Her pain increased with ambulation, prolonged sitting or lying on her right side. Pain decreased with standing or lying supine. She trialed short courses of ibuprofen and topical menthol gel without improvement. Past medical history revealed hypopituitarism, delayed puberty and adrenal insufficiency. Past surgical history included ligation of a patent ductus arteriosus and a left nephrectomy in infancy without complications. Exam was notable for antalgic gait and tenderness over right ASIS and AIIS. Passive ROM of the right hip was limited in all directions. Log roll test was negative. FADIR, hip scour, and Stinchfield tests were positive only on the right, but FABER was positive and reproduced groin pain bilaterally. Hip imaging demonstrated delayed closure of the growth plates of the femoral heads and slipped capital femoral epiphysis bilaterally. Brain MRI showed ectopic posterior pituitary gland with a hypoplastic anterior pituitary and non-visualized pituitary stalk.

Assessment/Results: The patient was diagnosed with bilateral slipped capital femoral epiphysis secondary to panhypopituitarism, low estrogen, and vitamin D deficiency. Bilateral SCFE was corrected with in situ screw fixation and the patient underwent post-op physical therapy.

Discussion: Traditionally, SCFE is a common cause of hip pain in adolescents usually between 8-15 years of age. Atypical SCFE is seen in cases associated with endocrine disorders, renal failure osteodystrophy or radiation to the pelvis.

Conclusion: It is imperative to maintain a broad differential and consider seemingly unrelated past medical history when creating a differential diagnosis to guide appropriate work-up.

Krill, Michael

Understanding fatigue and timing of ACL injuries in NFL games with snap counts and game number at time of injury

Michael K. Krill, MD, ATC[1], Nathan D. Schilaty, DC, PhD[2,3,4], Matthew L. Krill[5], Timothy E. Hewett, PhD[6,7]

[1]Division of Physical Medicine & Rehabilitation, Department of Neurology, Washington University in Saint Louis, Saint Louis, Missouri; [2]Sports Medicine Center, Mayo Clinic, Rochester, Minnesota; [3]Department of Physiology & Biomedical Engineering, Mayo Clinic, Rochester, Minnesota; [4]Department of Physical Medicine & Rehabilitation, Mayo Clinic, Rochester, Minnesota; [5]Division of Athletic Training, School of Health and Rehabilitation Sciences, Ohio State University, Columbus, Ohio; [6]Sparta Science, Menlo Park, California; [7]The Rocky Mountain Consortium for Sports Research, Edwards, Colorado

Category: Musculoskeletal and Sports Medicine

Objective:
Anterior cruciate ligament (ACL) ruptures are devastating and potentially career-ending injuries. Due to a noted increase in incidence decades ago, numerous changes were implemented that included prevention programs/neuromuscular training. The purpose of this study was to further understand the timing of ACL injuries to evaluate the potential role of fatigue.

Design: Retrospective review

Setting: National Football League (NFL) regular and post-season games

Participants: NFL athletes who sustained ACL injuries

Intervention: Not applicable

Main Outcome Measures: Descriptive statistics and details of athletes who sustained an ACL injury during a regular or post-season game including position, season, game of injury, and total snap count in the game of injury.

Results: 187 ACL ruptures were identified via NFL official game and injury reports, news and sports articles, and interviews from the 2012-13 to 2019-20 regular and post-season games. Overall (n=187) ACL injuries occurred at a median total snap count of 20 (interquartile range (IQR): 10-40 snaps). Offensive players (n=88) were injured at a median snap count of 24 (IQR: 11-43 snaps); whereas, defensive players (n=96) were injured at a median snap count of 20 (IQR: 10-36 snaps). Over the eight seasons monitored, the mean single team offensive snaps per game was 63.94 (SD:3.07).

ACL injuries (numbered 1-16 for regular season games, and 17-20 for subsequent potential post-season games) at a median game number of 7 (IQR: game 5-12, mode: game 5). There was an average of 23.75 ACL injuries over eight regular and post-seasons (SD: 4.44, median: 22, IQR: 20.25-28). There was a mean of 10.88 (SD:2.98) ACL injuries in pre-season games.

Level of Evidence: IV

Conclusion: ACL injuries had a similar early in game median total snap count between overall, offensive, and defensive position groups. ACL injuries in the regular and post-season were increased in the first half of the regular season.

Liu, Angela

Botox Injections for Migraine with Concomitant Face Pain

ABSTRACT: Facial pain is a common yet poorly understood entity and can be the cross point for many specialists, including dentistry, ENT, and neurology. Face pain can occur concomitantly with migraine, and notably, this subset of patients has more severe migraines that are difficult to treat. In this case series, we performed a retrospective chart review in 10 adult patients receiving Botox injections in the lateral canthus (V1), malar (V2), or masseter (V3) regions, in addition to standard injection sites for migraine. We determined if their facial pain was reduced in both severity and intensity post-Botox, with 50% being considered a clinically significant reduction. We also performed a descriptive analysis to characterize the clinical features of the facial pain. Following Botox, 70% of patients described a clinically significant reduction in pain. Most participants had bilateral facial pain (70%), with most patients describing facial pain in the V1 and V3 distribution (50% of bilateral pts) and V1 and V2 distribution (50% of bilateral pts). We hypothesized that Botox injections in the trigeminal distribution have a synergistic effect on the head pain associated with migraine via peripheral desensitization of trigeminal afferent neurons, which ultimately dampens central pain mechanisms.

Magsi, Shahvaiz

Subcortical T2/FLAIR Hypointensity and Diffusion Restriction-Usual and Unusual MRI findings of Hyperglycemic Seizures

Abstract:

Commonly reported MRI findings in hyperglycemia induced encephalopathy and seizures include transient cortical T2 hyperintensity, restricted diffusion, and often gyral and/or adjacent leptomeningeal contrast enhancement. We report the case of a 55 year old male with no known past medical history who came in with hypertension to SBP 190s and hyperglycemic to 443, presenting with several days of visual and auditory hallucinations, subsequently witnessed to have a seizure in the ED with left gaze deviation and left arm shaking progressing to generalized shaking followed by a postictal state. MRI brain with and without contrast revealed a region of cortical T2/FLAIR hyperintensity with subcortical T2/FLAIR hypointensity and associated diffusion restriction in the temporal/parietal lobes. Also noted was a region of curvilinear focus of contrast enhancement in a gyrus and adjacent sulcus in the right inferior lobule. Postcital EEG obtained showed sharply contoured right parieto-occipital slowing that correlated with the MRI findings. Hyperglycemia induced MRI findings of subcortical T2 hypointensities have been reported, seen in both ketotic and non ketotic hyperglycemia. Our case aims to reaffirm this neuroradiological finding as a “hallmark” in hyperglycemic seizures.

Ray, Christopher

Probable CAA-RI in the Setting of Sitravatinib Chemotherapy

Christopher Ray, MD; Kalen Dionne, MD PhD

Abstract:

A 67-year old man with liposarcoma developed chronic headaches, subacute encephalopathy, and suffered a single seizure while receiving sitravatinib, a small molecule inhibitor of receptor tyrosine kinases (RTKs). MRI revealed vasogenic edema and chronic lobar microbleeds. The patient met criteria for probable Cerebral Amyloid Angiopathy Related Inflammation (CAA-ri) based on history and imaging findings. Lumbar puncture was unremarkable except for elevated phosphorylated tau to amyloid beta-42 ratio. Frontal lobe biopsy revealed intact grey matter vasculature with positive amyloid immunostaining and surrounding areas of microglial proliferation and astrocytosis. Sitravatinib was discontinued and the patient received high-dose steroids resulting in rapid clinical improvement and resolution of edema on MRI. To our knowledge this is the first case of neurological autoimmunity reported in a patient receiving sitravatinib. Given the known role of RTKs in immune regulation, we speculate that sitravatinib may have contributed to development of CAA-ri. In conclusion: (1) care should be taken when initiating immune modulating therapy in patients with underlying amyloid pathology, (2) early recognition of CAA-ri combined with discontinuation of immune modulating drugs and initiation of high-dose steroids can improve clinical outcome, and 3) further studies are needed to define the role of RTKs in the development of CAA-ri.

Rodrigo, Shashika

Remote Electrical Neuromodulation (REN) treatment in Patients with Chronic Migraine: A retrospective case series

Shashika Rodrigo, MD, David Lardizabal, MD, MBA, FAAN

STUDY PURPOSE/BACKGROUND: Chronic migraine is a disabling condition which affects a significant proportion of the global population, from 1.4 - 2.2% (1). Patients with chronic migraine suffer from headaches which occur on at least 15 days per month for more than 3 months. Of these headache-days, at least 8 per month have features consistent with migraine (2). Currently, pharmacological treatments are used first-line to treat chronic headaches, including triptans, NSAIDs and gepants (3, 4). However, overuse of these medications can lead to medication-overuse headaches (5). Various non-pharmacological treatments have been explored for patients with migraine, including transcranial magnetic stimulation, vagus nerve stimulation, and more recently, remote electrical neuromodulation (REN) but patients with chronic migraines are often excluded from these studies (6-8). Further studies to better elucidate the effectiveness of REN, such as Nerivio Migra, in patients with chronic migraine would be useful in treating this population with headaches refractory to multiple medications.

METHODS: A retrospective chart review from 10/1/2020 to 3/1/2021 was performed to find patients with a diagnosis of chronic migraines, who were prescribed Nerivio. Of these participants, we reviewed their usage of the Nerivio device as well as the questionnaires they routinely receive after using the device, which detail how participants used the device, their response to the device and any adverse events that occurred with device use.

RESULTS: The case series included 6 patients who see a headache specialist at an academic medical center with a clinical diagnosis of chronic migraine, who have failed several abortive and preventative treatments. The average age of participants was 41, and 5 out of 6 participants were female. Participants reported an average of 6 severe migraines per month, with median headache duration of 6.5 hours. The participants reported 64 total uses of Nerivio, with a median of 5 uses. Of these 64 uses, 15% were preceded by intake of abortive headache medications within 2 hours. Medications included Ubrogepant, Oxycodone, Frovatriptan, and Lamsitidan. Average severity of headache prior to Nerivio use was 4 out of 5 on a scale from 1 to 5, with 5 being most severe headache and 1 being a mild headache. Average headache severity 2 hours after use of Nerivio was 2 out of 5. Average headache severity 24 hours after Nerivio was 2 out 5. None of the participants reported adverse events with the device.

CONCLUSIONS: The efficacy of Nerivio has been previously demonstrated in patients who met criteria for migraine (8). this case series, Nerivio was effective in reducing headache severity after 2 hours and sustaining headache relief after 24 hours in participants with chronic migraines. In 15% of uses of the product, it was used as an adjunctive therapy with abortive medications. Comments on usability by several participants suggest that Nerivio may be more effective as adjunctive therapy or to delay use of abortive therapy in patients with chronic migraines.

Nerivio may provide an alternative option for patients with contraindications to headache medications, reduce incidence of medication overuse headaches and provide a non-opioid alternative for headache management. Limitations of this study include small sample size and lack of placebo group.

Stupnitsky, Alan

Sacrococcygeal chordoma in a 53-year-old female with Stickler syndrome: Related entities?

Case Diagnosis
Chordoma in a patient with hip pain and Stickler syndrome

Case Description
A 53-year-old female with Stickler syndrome presented to an outpatient musculoskeletal physiatry clinic for six months of deep left groin, lateral hip, and posterior pelvic pain that interfered with ambulation. Her sister also has Stickler syndrome and was previously diagnosed with a chordoma. The patient's physical exam was notable for thoracic scoliosis and severe left hip stiffness, with reproduction of pain during hip motion. Radiographs revealed mild hip osteoarthritis. A subsequent noncontrast left hip MRI revealed severe hip osteoarthritis and a sacrococcygeal mass. Mass biopsy demonstrated a chordoma. She underwent wide resection with removal S3-S5 spinal nerves. Her post-operative course required inpatient rehabilitation for sitting precautions, urinary retention, constipation, and neuropathic and incisional pain. Post-operatively, her hip pain persisted, and she proceeded with total hip arthroplasty.

Discussion
Stickler syndrome is a disorder attributed to pathogenic collagen genes. It can predispose to joint laxity, scoliosis, osteoporosis, and facial abnormalities. Chordomas are notochord remnant tumors in the spine. These two rare disorders are not known to be associated with one another. To our knowledge, these are the first two reported cases of chordoma in patients with Stickler syndrome. However, cartilage and the notochord express similar genes, so aberrant collagen gene expression in the notochord may lead to inappropriate notochord development and predispose patients to chordomas. Although the patient's chordoma was likely unrelated to her presentation for hip pain, physiatrists should be aware of this potential association since Stickler syndrome can predispose patients to musculoskeletal conditions that are often managed by physiatrists.

Conclusions
Stickler syndrome can predispose to multiple complications that require physiatric care due to abnormal collagen deposition. Treating physiatrists should be aware of a possible association with chordomas and screen for myelopathy symptoms accordingly.

Stupnitsky, Alan

Upper Extremity Deep Vein Thrombosis in a Healthy 30-year-old Woman: A Case Report

Case Description:

The patient presented with spontaneous, insidious left arm pain, and paresthesia for 3 months. Medical history includes remote left shoulder dislocation without complication. She was seen by rheumatology 6 months prior, diagnosed with Sjögren's disease, started on apixaban and prednisone. Imaging demonstrated left internal jugular and subclavian deep vein thrombosis (DVT) near the clavicle. Work-up included EMG, MRI of brain and cervical spine that were unremarkable.

The patient endorsed dull, aching left shoulder pain that was moderate in intensity with weakness and numbness radiating down the left arm that involved the entire hand. Symptoms were exacerbated with overhead activities. Diffuse tenderness to palpation over left pectoral musculature. Bilateral shoulder range of motion was symmetrical and within normal ranges. Examination positive on the left for Tinel's sign at pectoralis minor and elevated arm stress test. The patient was referred to physical therapy (PT) and referred to vascular surgery for concern for neurogenic thoracic outlet syndrome (TOS). MRA revealed severe narrowing of the left subclavian vein with arms abducted, not present with arms at her side. No evidence of thrombosis noted.

Assessment/Results:

She completed PT for TOS with limited improvement in her symptoms. Due to lack of progress with activity modification and PT, she was referred to vascular surgery for consideration of subclavian vein decompression.

Discussion:

Paget-Schroetter Syndrome, also known as "effort-induced thrombosis" is a form of upper extremity DVT that typically occurs in the axillary or subclavian veins of young, otherwise healthy individuals after reported vigorous activity. The incidence of this rare condition is 2.03 per 100,000 people and may be a presenting sequela of TOS.

Conclusion:

Paget-Schroetter Syndrome is a rare condition that can present with activity related upper extremity DVT and TOS symptoms.

Tang, Caroline

Influence of Culture Environment on Microglia Identity

Abstract:

Microglia is the resident tissue macrophage within the CNS and is known to exhibit unique marker expression profile. Microglia can be readily isolated from brain tissue, and past consensus has been that microglia cells continue to display unique morphological and histochemical signatures in vitro, when compared to other tissue or bone marrow-derived macrophages. Here we present preliminary findings that peritoneal macrophage cultured in microglia medium, instead of traditional macrophage medium, undergo morphological and biochemical transformations to resemble microglia in vitro. These findings highlight the fluidity in myeloid cell identities and may assist in the understanding of the immune response to neurological conditions such as brain tumor or injury, which frequently attract circulating myeloid cells to the CNS.

Williams, Jonathan

An Evaluation for False Localization of Temporal Lobe Seizures on Surface EEG Using Intracranial Foramen Ovale Electrodes

Abstract:

EEG monitoring is an essential part of standard epilepsy evaluation. Yet, only 19% of auras and 10% of subclinical seizures could have “surface” (scalp) EEG expression (Risinger et al.). Advancements in surgical techniques have expanded capability of EEG monitoring beyond scalp electrodes to allow for intracranial monitoring. Intracranial monitoring is defined by placement of electrodes inside the skull (i.e. grid, depth electrodes) for direct monitoring of brain waves. Some studies have reported 20–40% false lateralization in those with predominant lateralized interictal finding on scalp EEG. Using both surface and depth electrodes, many seizures that had no scalp EEG expression at the onset when they have already appeared on depth electrodes and scalp EEG showed bilateral and/or non-lateralizing changes. Further, one study with 91 patients undergoing intracranial EEG, localization was achieved based on data obtained from surface electrodes alone (in 29 patients), depth electrodes alone (in 13 patients), or a combination of both surface and depth electrodes (in 42 patients) (Nagahama Y, Schmitt AJ, Nakagawa D, et al). Here, an interesting clinical case of temporal lobe epilepsy is presented showing good localizing value from intracranial monitoring when used to augment data from scalp monitoring.

Wren, Mary

Quality of documentation in post-stroke follow-up visits in the neurology resident continuity clinic

Mary Wren, MD Lauren Langford MSN, RN, Gabriela de Bruin MD
Department of Neurology, Washington University in St. Louis

Background: Post-hospitalization stroke follow-ups are increasingly seen in the resident continuity clinic. The American Heart Association has several metrics and guidelines to assist physicians with optimizing care for these patients. These were not previously formally integrated into the resident continuity clinic.

Methods: Each resident reviewed the charts of patients evaluated seen in follow-up for stroke in the first half of the academic year (July-November 2020), assessing how their documentation aligned with selected outcome measures on a standardized worksheet. This process allowed for resident-directed self-assessment of care provided to their patients After the initial survey, residents attended an educational session about these measures and an electronic medical record template was created and implemented to help residents record this information for management of patients with recent stroke. The self-assessment worksheet was again collected for patient encounters following implementation (December 2020-March 2021) and responses were compared.

Results: Education about documentation and management of stroke follow-up visits and inclusion of a clinic note template trended toward improvement in documentation of management of stroke follow-ups. This included documentation of management strategy, discussing lifestyle changes (E.g. tobacco/drug use), and communication with other providers. After the intervention, there was a trend for residents to be more confident in management of stroke patients.

Conclusion: This system formalized integration of select standards for the management of patients with recent stroke in the resident continuity clinic, with the goal of promoting knowledge and application of quality care guidelines in the management of patients.