ALABAMA ACADEMY OF NEUROLOGY

AAN 2021 Annual Conference Poster Presentation

Abstract 21-01

Title: Demographic and clinical associations with Neuromyelitis Optica Spectrum Disorder in an academic medical center

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Objective: Understand the demographic and clinical associations with Neuromyelitis Optica Spectrum Disorder at an academic medical center.

Background: Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare, inflammatory CNS syndrome, which, left untreated, may result in significant disability or even death. Due to its low incidence and prevalence, the importance of demographics on disease risk and outcome remains incompletely described. Previous research has shown that Blacks may be disproportionately at risk of NMOSD and may experience greater disability. Alabama and surrounding states have some of the highest percentages of Black residents in the U.S. This provides a unique opportunity to examine epidemiology of the disease.

Methods: All clinical records at the University of Alabama at Birmingham with an NMOSD diagnosis were found using the i2b2 search engine. A retrospective chart review was conducted to collect demographics, BMI, antibody status, and details of the clinical course. Likelihood ratio Chi-square test or Fisher's Exact (FE) test was used for comparisons, with $p<0.05$ considered meaningful. Analysis was completed using JMP Pro 15 (Cary, NC).

Results: A total of 121 patients (84.3% female) were found to have a diagnosis of NMOSD. Of those, 60.3% were Black, 25.6% White, 6.6% Asian, 5.8% Other, and 1.7% Hispanic/Latino. For context, the population of the state of Alabama is 26.6% Black. Blacks presented at a younger age than Whites (45.8 vs 55.1 years of age, $p=0.0034$). Transverse myelitis (53.9%) was the overall most common presenting symptom, followed by optic neuritis (41.4%) and area postrema syndrome (4.8%). Presenting syndromes did not significantly differ by race.
Aquaporin-4 (AQUP4) antibodies were present in 68.6% of cases, while 16.5% had myelin oligodendrocyte glycoprotein (MOG) antibodies, and 14.9% were seronegative. Race was associated with antibody type ($p = 0.0008$): A higher proportion of Blacks were AQUP4 positive compared to Whites (79.5 vs. 41.9%); while Whites were more likely to be MOG positive (35.5 vs 9.6%) and seronegative (22.6 vs 11.0%). There were no significant

differences in disability status by race, as determined by lasting ambulatory or visual impairment.

Conclusion: This analysis shows that Blacks are over-represented among NMOSD patients in this single-clinic study. There are significant differences in antibody status and type among Black patients compared to other Whites, while clinical presentations did not differ by race. Further research is needed to further characterize these clinical differences and response to treatments.

Acknowledgment: This research supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under award number UL1TR003096. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2021 Annual Conference Poster Presentation

Abstract 21-02

Title: A Case of Overlapping Clinical Syndromes in a Patient with Anti-NMDAR, GFAP, and NMO Antibody Positive Disease

Authors: Rebecca L. Massey, Vanessa Sui, M.D., Shruti Agnihotri, M.D.

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Objectives: To describe a unique case of overlapping clinical syndromes due to anti-NMDAR, GFAP, and NMO antibody positive autoimmune CNS disease.

Background: Anti-NMDA receptor (anti-NMDAR) encephalitis is associated with a characteristic clinical syndrome of prominent psychiatric symptoms, disordered sleep, cognitive changes, dyskinesias, and seizures. Neuromyelitis optica spectrum disorders (NMOSD) represent a full spectrum of CNS demyelinating disorders, typically affecting the optic nerves and spinal cord. NMOSD is associated with antibodies against aquaporin-4 (AQP4), a channel protein prevalent in spinal cord gray matter, periventricular and periaqueductal areas, and astrocytic foot processes at the blood-brain barrier. The presence of autoantibodies against glial fibrillary acidic protein (GFAP), while less well-defined, has been identified as a marker for relapsing autoimmune meningoencephalitis.

Case Summary: A 20 year old woman presented with 1 week history of diplopia and decreased hearing in the left ear. Diplopia was described as binocular and vertical. She denied pain with eye movements, change in visual acuity, headaches, nausea, vomiting, numbness, and tingling. Past medical history was notable for a 9-month history of sudden onset depression, executive dysfunction, personality changes, and a "psychotic episode" requiring hospitalization in November 2020. No imaging was performed at the outside hospital, and patient had been diagnosed with major depressive disorder, borderline personality disorder, and an eating disorder at that time and was managed with anti-psychotic medications. On examination, she was noted to have a left CN IV palsy, nystagmus on horizontal gaze, and diffuse hyperreflexia. MRI brain with and without contrast showed several areas of patchy bilateral periventricular, periaqueductal, and basal ganglia FLAIR hyperintensities with some diffusion restriction and patchy enhancement. CSF analysis was notable for WBC count of 8/mm^3, protein of 54mg/dl, glucose of 54mg/dl, and >5 unique oligoclonal bands. She was empirically treated with high dose steroids and PLEX for suspected autoimmune inflammatory CNS disease, with trace symptomatic improvement. Subsequently, remaining CSF studies returned, revealing positive antibodies against NMDAR, AQP-4, and GFAP. She was discharged home on oral prednisone taper. MRI pelvis did not identify any ovarian teratoma. Upon follow up in clinic, patient showed

some improvement in vision and mood with near resolution of diplopia, but lack of motivation, disordered sleep, and executive dysfunction persists, causing her to remain partially dependent on her parents.

Discussion: This case demonstrates that while rare, overlapping neuronal antibody syndromes is an important consideration in patients with vexing clinical presentations and/or imaging that is not classic for one individual syndrome. The imaging appearance in this case is not typical of NMOSD or anti-NMDAR encephalitis. Thorough history, physical exam, laboratory studies, and imaging can provide clues that allow for empiric treatment of suspected mixed autoimmune CNS syndromes, even while key studies are pending. Overlapping neuronal antibody syndromes are more likely to be due to autoimmunity than paraneoplastic processes. The case also highlights both the challenges in and importance of prompt diagnosis and treatment of these diseases.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2021 Annual Conference Poster Presentation

Abstract 21-03

Title: Functional Connectivity Between Cerebral Cortex and GPE: Parallel Investigations from Mouse Connectome and Humans During DBS Surgery

Authors: Adam Bashir, Harrison Walker M.D.

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Objective: 1. Present data supporting the existence of a primary motor cortex to GPe projection in mammals.

Background: Basal ganglia, thalamus, and cerebral cortex form dense interconnected brain networks that control both normal and pathological movements. Here we examine functional connectivity between frontal cerebral cortex and basal ganglia with data from the Allen Brain Institute mouse connectome and parallel experiments in a patient undergoing deep brain stimulation surgery (DBS) for Parkinson's disease. Results from these studies could inform ideas about basal ganglia pathophysiology, the therapeutic mechanism of DBS, and potential control signals for future closed-loop stimulation devices.

Methods: The Allen Brain Institute connectome introduces adenovirus carrying green fluorescent protein into 213 anatomically distinct brain regions in the mouse brain. This public data resource allows high dimensional visualization, quantification, and normalization of first order connectivity among these brain regions in the mouse. Neuronal tracts with larger normalized projection volumes suggest greater monosynaptic functional connectivity. In parallel, we are analyzing cortical potentials evoked by globus pallidus interna and externa (GPi and GPe) stimulation during DBS surgery in patients with Parkinson disease as part of an ongoing IRB-approved protocol investigating the therapeutic mechanism of DBS.

Results: Projection volumes were collected for primary motor cortex neurons to deep brain structures of interest in 11 experiments from mice. We identified significant projections from primary motor cortex to both GPe and GPi, to a greater extent on the ipsilateral (0.33 and 0.08, respectively) versus the contralateral (0.05 and 0.0015, respectively) hemisphere. In contrast, primary motor cortex projections to visual cortex, a known target with minor projections, is only 0.006. Further, primary motor cortex projections to STN (the well-established cortico-subthalamic or 'hyperdirect' pathway) was 0.06. Ongoing analyses are investigating and validating whether these novel projections are present in humans undergoing DBS surgery for Parkinson's disease.

Discussion: Primary motor cortex neurons sends direct monosynaptic projections to bilateral GPi and GPe in the mouse. Identification and validation of similar connections

in humans undergoing DBS surgery could add to existing knowledge about cortical-pallidal connectivity in humans. These novel potentials could eventually be used as a control signals to guide therapy with emerging closed loop and directional DBS device technologies.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2021 Annual Conference Poster Presentation

Abstract 21-04

Title: Cryptogenic Strokes

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Objective: Understand the importance of a comprehensive stroke etiology investigation
Stimulate the inclusion of unusual differential diagnosis in common CNS pathologies
Display an interesting case of Acute Ischemic Stroke

Background: Stroke is the fifth cause of death in America and one of the leading causes of disabilities [1]. Ischemic Stroke mechanisms are usually classified using the TOAST criteria [2]. The etiology of ischemic stroke affects prognosis and outcome. Among the stroke types, approximately 30% are deemed cryptogenic due to undetermined etiology after standard evaluation [3]. Moreover, the use of therapeutic agents and recreational drugs that affect vascular tone are commonly linked to Reversible Cerebral Vasoconstriction Syndrome, which is an uncommon etiology of ischemic strokes [4]. We aim to stimulate the broadening of differential etiologic diagnosis and to display a challenging case of acute ischemic stroke.

Case Summary/Studies: 57 year-old Caucasian female with no significant past medical history who presented to the ED complaining of right sided weakness involving face, arm and leg that lasted for 10 hours. She also reported associated word finding difficulty. On arrival to the ER, NIHSS was 0. Acute stroke workup revealed perfusion deficits involving the left MCA territory, CTA with severe bilateral stenosis of the Middle cerebral arteries and CT head with remote basal ganglia and centrum semiovale. She was admitted to the stroke unit and subsequent investigation revealed recent infarcts in the left centrum semiovale on MRI. Her lipid panel and HbA1c were within normal limits, but UDS was positive for Amphetamines. She was also found to be hypertensive with SBP in the 170's. Upon further investigation, she reported long history of tobacco use and recent use of amphetamine.

Results:
HR: 86 RR: 18 BP: 171/59
HDL 48
LDL 132
Cholesterol 189
HbA1c 5.5
UDS Amphetamines
ECHO – No thrombus, atrial dilatation, wall motion abnormality or PFO
MRI/CTA - infarcts in the left centrum semiovale

Discussion: Ischemic strokes can be very challenging from both diagnostic and therapeutic standpoint. The investigation of stroke etiologies is a laboring and expensive process that includes different imaging modalities of the brain, its vessels, and the heart. However, we often face a diagnosis of cryptogenic strokes. In this case we presented a middle-aged female who was admitted to our service after she experienced transient right sided weakness and expressive aphasia, which had resolved on arrival to the ER. Workup revealed uncontrolled systemic hypertension, extensive intra and extra-cranial atherosclerosis, subcortical scattered infarcts on MRI. History was positive for tobacco and illicit drug use which was confirmed by patient and an UDS positive for Amphetamines. Lipid panel and Glycated hemoglobin within normal limits. The pattern of her strokes on MRI opens up discussion for different possibilities of its etiology such as Large vessel atherosclerosis, Small vessel occlusion, Watershed infarcts (other etiology) and Cardioembolism. Her history of recent use of Amphetamine also raises suspicion for vasoconstricting syndromes such as RCVS. In summary, a thorough work-up for patients with vascular neurological diseases is a crucial step in the process of the whole stroke care chain and it is necessary to keep an open mind to unusual etiologies to deliver optimal therapy and secondary prevention.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2021 Annual Conference Poster Presentation

Abstract 21-05

Title: Transverse Myelitis associated with COVID-19 in an adult

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Objective: To describe a case of transverse myelitis associated with mild COVID-19 in an adult with improvement after treatment, suggesting role of SARS-CoV-2 in development of post-infectious neurologic complications.

Background: Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was declared a pandemic in March 2020. COVID-19 has infected about 200 million people worldwide and is an ongoing global health emergency. Neurological manifestations of COVID-19 are being increasingly recognized. Here, we present a case of transverse myelitis associated with COVID-19.

Case Summary: A 56-year-old man from Mississippi with hypertension, coronary artery disease, and obstructive sleep apnea with recent COVID-19 diagnosis presented to a community hospital after recurrent falls in the setting of four months of progressive bilateral arm and leg weakness with urinary retention. He began experiencing hyperesthesia, imbalance, and weakness from the neck down with prominence in the lower extremities two weeks after recovery from a mild COVID-19 illness. He also had pins and needles with numbness in all extremities that later involved his middle and lower torso. He described mild weakness as his new baseline with intermittent worsening every two weeks. During flare-ups, he noted his legs "give out," which at times included inability to rise from a seated position or ambulate. His urinary retention was initially attributed to BPH, resulting in an UroLift procedure; yet retention persisted. He relied on self-catheterization prior to hospitalization. Patient complained of depression but denied visual disturbances, dysarthria, dysphagia, bowel changes, facial sensory/motor deficits, headache, or vertigo. Initial CSF studies resulted in a protein of 154 mg/dl, glucose of 56 mg/dl, and white blood cell count of 7/mm^3. Before transfer to UAB, he received one dose of IV Solu Medrol which was discontinued due to severely worsening weakness.

Results: On arrival, neurologic exam was remarkable for bilateral upper extremity strength 3/5, bilateral lower extremity strength 1-2/5 and diffuse hyperesthesia from the level of T-4 and below but otherwise no diminished sensation appreciated with light touch, pinprick, or temperature. Patient required total assistance for all ADLs and was unable to ambulate independently. MRI Brain, C-spine, and T-spine with and without contrast showed T2 Flair hyperintensity in a longitudinally extensive pattern extending

from the lower medulla into the level of T-3 with associated patchy enhancement and intrinsic cord edema. CT Chest showed no evidence of sarcoidosis. SARS-CoV2-RT-PCR obtained from nasopharyngeal swab was negative. Repeat lumbar puncture was performed revealing protein level of 278 mg/dl, glucose level of 61 mg/dl, red blood cell count of 1502/mm^3, and white blood cell count of 18/mm^3 with lymphocytic predominance (lymphocytes 58%, monocytes 29%, PMNs 12%, other 1%). CSF testing for culture and routine microbial stains, HSV PCR, VZV PCR, CMV PCR, AFB stains, and cryptococcal antigen were negative. Serum demyelinating panel was negative. He was diagnosed with post-infectious transverse myelitis secondary to COVID-19. He was treated with five sessions of plasmapheresis with marked interval improvement. Upon discharge to an inpatient rehabilitation facility, he was ambulating with assistance with strength 4/5 in the lower extremities.

Discussion: Inflammatory and autoimmune diseases are associated with viral illnesses. SARS-CoV-2 is also associated with various post-infectious complications including Transverse myelitis, Guillain-Barre syndrome and Acute Demyelinating Encephalomyelitis. While causation remains difficult to prove, our case suggests that our patient's transverse myelitis was precipitated by COVID-19 as the onset of neurologic symptoms was 2 weeks after COVID-19 diagnosis and no other etiology for myelitis was identified. Furthermore, his condition improved with plasmapheresis which suggests an immune mediated cause. This case adds to the growing body of evidence of neurologic complications associated with COVID-19 and the need for neurologists to be vigilant of neurological illnesses during the current pandemic.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2021 Annual Conference Poster Presentation

Abstract 21-06

Title: Ictal Gerstmann-like Syndrome as the presentation of simple partial seizure activity in a 54-year-old

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Objective: To present an unusual seizure presentation and explore its pathophysiologic presentation, diagnostic workup, differential diagnosis, and treatment.

Background: Gerstmann syndrome is characterized by the tetrad of acalculia, agraphia, finger agnosia, and left-right disorientation. It is caused by a lesion of the angular gyrus, near the junction of the parietal and temporal lobes. Gerstmann syndrome presents most commonly as the result of a stroke or TIA, but it may rarely present as an epileptic manifestation.

Case Summary: In this case report, we present a 54-year-old right-hand dominant speech therapist with no history of seizures, strokes, or migraines. Our patient presented to the emergency department with reports of confusion, left-temporal headache, and "dizziness". On the morning of her presentation, the patient attempted to call into work sick, but upon picking up the phone, she did not know how to use it and was brought to the hospital by her husband, who stated that she was having trouble finding words. The patient was oriented to person and place but not to time; she was also unable to identify the current president. Her presentation was unremarkable for weakness, numbness, or paresthesia.

When examined in the emergency department, it was discovered that the patient was experiencing agraphia. When asked to write her daughter's name, the patient was unable to correctly spell the name and was noted to have particularly sloppy handwriting. Additionally, the patient was unable to unable to count backwards from 100 in increments of 7, and she was also unable to identify the date, despite her knowledge that her husband's birthday was seven days away on the 21st of that month. On repeat exam of the patient several hours later, she was able to correctly write her daughter's name in neat, cursive writing.

Results: EEG confirmed focal, intermittent epileptic activity of the left cerebral hemisphere with periods of on and off seizure activity, likely explaining the drastic variations in her writing abilities. While yet unconfirmed, the patient's venous anomaly is perhaps responsible for this later-in-life seizure presentation. The patient received Levetiracetam (Keppra) in the emergency department and was continued on this

medication at discharge. The patient was seen in clinic for follow-up the following week and presented with resolution of her symptoms and the dosage was slightly increased.

Discussion: The differential diagnosis for this patient included stroke, TIA, complex migraine, seizure, psychogenic non-epileptic seizures, and anxiety. CT and MRI were negative for stroke, but a small venous anomaly of the left frontal lobe was identified. Labs were otherwise normal. With seizure, P-NES, and anxiety now the highest on the differential, an EEG was ordered, and the patient was started on levetiracetam (Keppra).

This patient's presentation was most noteworthy for its very specific and unorthodox seizure manifestations. It demonstrates that the absence of more traditional positive symptoms of epilepsy may not always be relied upon to reach a diagnosis. Agraphia, acalculia, and agnosia, thought more of as CVA sequelae, may indeed be the result of epileptic activity in the same or similar areas. For this reason, and so as not to allow intermittent seizures to run free, EEG can be instrumental in clarifying a diagnosis and should be employed concurrent to or following imaging modalities that have ruled out CVA.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2021 Annual Conference Poster Presentation

Abstract 21-07

Title: Assessing the Role of Slow Wave Sleep on Longitudinal Cognitive Performance in Parkinson's Disease

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Objective: Investigate whether slow wave sleep (SWS, i.e., deep sleep or non-REM stage 3 (N3) sleep) predicts longitudinal cognitive change in persons with Parkinson's disease (PwP).

Background: Parkinson's disease (PD) is the most common neurodegenerative motor disorder of aging (Abbas et al., 2018). Although PD diagnosis requires cardinal motor symptoms, quality of life is significantly affected by non-motor features, including sleep disorders and cognitive impairment (Todorova et al. 2014). Slow-wave activity (0.5-4Hz) during N3 is associated with cognitive decline and age-related neural plasticity in healthy adults (Tononi and Cirelli 2014). Indeed, we previously reported in a cross-sectional study that the percentage of SWS correlated with global cognition in PD as well (Wood et al. 2021). However, whether SWS predicts long-term cognitive decline in PD is unknown. Therefore, to address this critical question, we examined whether SWS predicts performance on a level II neurocognitive battery, as defined by the Movement Disorders Society Task Force on PD-mild cognitive impairment (PD-MCI) (Litvan et al. 2012) three years after the initial sleep study.

Methods: Thirty-nine PwP underwent polysomnography (PSG) and completed a comprehensive neurocognitive battery comprised of tests of global cognition (MoCA), and at least two tests in each of the following domains: executive function, attention/working memory, language, visuospatial function, processing speed, and memory. Twenty-five participants also completed the comprehensive neurocognitive battery three years after baseline and those participants were included in this interim analysis. Raw scores for each cognitive test were transformed into z-scores using normative data. The z-scores for each domain were averaged to obtain domain scores. The Cognitive Composite Score (CSS; primary outcome) was obtained by averaging the domain scores. Summary statistics were calculated for baseline demographics and sleep parameters. Stepwise and linear regression were performed. This is an ongoing study and year-4 neurocognitive assessments are also planned.

Results: Demographics of the twenty-five participants at baseline were: 40% male; age: 62.5±8.4 (mean±SD); education: 15.75±2; duration of disease: 4.24±3.03 years; levodopa equivalent dose: 517±325 mg. At baseline, total N3 duration and percent were 53±34.2

minutes and 14.1±9.3%, respectively. Stepwise regression demonstrated that N3% at baseline accounted for 12% of the variance in change in CCS from baseline to year 3 and a linear regression model with the change in CCS as the dependent variable and N3% as the independent variable showed a trend toward significance (F=3.38; p=0.079). As secondary analysis, N3% also showed a trend toward being predictive of change scores in executive function (p=0.090), and attention/working memory (p=0.082). N3% was not a significant predictor of longitudinal change in memory, language, visuospatial or processing speed domains.

Discussion: This ongoing study suggests that slow wave sleep may influence longitudinal cognitive performance and opens the possibility that interventions to improve sleep might also improve cognitive function in individuals with PD. In addition, this novel work suggests that SWS, a noninvasive and widely accessible measure, may be used as a potential marker to evaluate the progression of cognitive decline in PD.

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