ALABAMA ACADEMY OF NEUROLOGY

AAN 2024 Abstract

Case Study Abstract 24-01

Title: Rituximab as an Abortive Therapy for Tumefactive Demyelination in Multiple Sclerosis

Presenting Author: Olivia Brookins, MS-3, University of South Alabama Frederick P. Whiddon College of Medicine

Additional Author(s): Caroline W. Howell, B.S., Olivia G. Brookins, B.S., A. Brooke Tarrant, B.S., Corinne E. Gautreaux, B.S., Daniel C. Lee, M.D., William Kilgo, M.D.

Introduction/Background: Tumefactive Multiple Sclerosis (MS) is a rare variant of MS which is notably more aggressive and produces more severe symptoms. The disease is characterized by the presence of a large demyelinating lesion in the setting of diagnosed MS. Additionally, Tumefactive MS is unique from traditional MS in both acuity of symptoms and responses to traditional treatment with higher resistance to standard medical therapy. Given the rarity and heterogeneity of response to typical treatments for MS, tumefactive lesions pose a challenge in therapeutic management. While steroids and plasma exchange are the mainstay of initial treatment, further management options are highly variable.

Description: We detail a 30-year-old woman who presented with an acute tumefactive lesion refractory to multiple steroid treatments and two rounds of plasma exchange. With continued progression despite these initial treatments, Rituximab was initiated and following two infusions the patient showed marked improvement with near complete remission of symptoms.

Discussion and Conclusion: Based on these results, Rituximab may offer promise as an abortive therapy for acute onset tumefactive demyelinating lesions.

References: Algahtani H, Shirah B, Alassiri A. Tumefactive demyelinating lesions: A comprehensive review. Mult Scler Relat Disord. 2017 May;14:72-79. doi: 10.1016/j.msard.2017.04.003. Epub 2017 Apr 9. PMID: 28619436.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2024 Abstract

Research Abstract 24-02

Title: Measuring in vivo mPFC Acetylcholine Tone in a Mouse Model of Narcolepsy

Presenting Author: Ajay Peddada, MS-3, University of South Alabama Whiddon College of Medicine

Additional Author(s): Ajay Peddada (1), Jinhwan Choi PhD (2), Christopher A Cano MD (3), Thomas E Scammell MD (2)

1: University of South Alabama Whiddon College of Medicine;

2: Department of Neurology, Beth Israel Deaconess Medical Center;

3: Department of Neurology, Brigham and Women's Faulkner Hospital

Introduction/Background: Narcolepsy Type 1 is a sleep disorder characterized by excessive daytime sleepiness and cataplexy due to a selective loss of orexin neurons in the lateral hypothalamus. These orexin neurons, which are implicated in the stabilization of sleep-state transitions, project to numerous brain areas, including the basal forebrain (BF) of the medial prefrontal cortex, which are implicated in wakefulness and cognition and whose activity may be altered in Narcolepsy. In our study, we examined whether cholinergic tone across the sleep/wake cycle is impacted by a loss of orexin neurons.

Methods: To this end, we employed a mouse model of Narcolepsy in which orexin-neurons were selectively ablated via administration of diphtheria toxin recombinant mice expressing the human diphtheria toxin receptor (DTR) driven by a prepro-orexin promoter (orexinDTR mice). We measured levels of acetylcholine (ACh) released by neurons in the BF via fluorescent G-protein-coupled receptor-activation-based (GRAB) ACh sensors recorded by fiber photometry. Additionally, we simultaneously measured EEG and performed video recordings to identify transitions in mouse sleep-wake states. We compared the levels of ACh in the BF between 6 wild-type and 5 orexinDTR mice in different sleep states. Finally, we plotted ACh levels against sleep state and spectral power in specific EEG frequency bands.

Results: We observed a decrease in peak ACh levels during wakefulness in orexinDTR mice before and after administration of diphtheria toxin and subsequent loss of orexin neurons. There was no difference in ACh levels averaged across entire sleep-states between orexinDTR and wild-type mice.

Discussion and Conclusion: Our findings suggest a neurobiological mechanism by which a loss of orexin-neurons leads to decreased wakefulness in Narcolepsy. Decreased cholinergic tone in the basal forebrain could be further explored to explain impaired cognition and diminished sustained attention via prefrontal cortex dysfunction in Narcolepsy.

References: Mahoney, C.E., Cogswell, A., Koralnik, I.J. et al. The neurobiological basis of narcolepsy. Nat Rev Neurosci 20, 83--93 (2019). https://doi.org/10.1038/s41583-018-0097-x

Xu M, Chung S, Zhang S, Zhong P, Ma C, Chang WC, Weissbourd B, Sakai N, Luo L, Nishino S, Dan Y. Basal forebrain circuit for sleep-wake control. Nat Neurosci. 2015 Nov;18(11):1641-7. doi: 10.1038/nn.4143. Epub 2015 Oct 12. PMID: 26457552; PMCID: PMC5776144.

Anaclet, C., Pedersen, N., Ferrari, L. et al. Basal forebrain control of wakefulness and cortical rhythms. Nat Commun 6, 8744 (2015). https://doi.org/10.1038/ncomms9744

Chen, L., Yin, D., Wang, TX. et al. Basal Forebrain Cholinergic Neurons Primarily Contribute to Inhibition of Electroencephalogram Delta Activity, Rather Than Inducing Behavioral Wakefulness in Mice. Neuropsychopharmacol 41, 2133--2146 (2016). https://doi.org/10.1038/npp.2016.13

Jing M, Li Y, Zeng J, Huang P, Skirzewski M, Kljakic O, Peng W, Qian T, Tan K, Zou J, Trinh S, Wu R, Zhang S, Pan S, Hires SA, Xu M, Li H, Saksida LM, Prado VF, Bussey TJ, Prado MAM, Chen L, Cheng H, Li Y. An optimized acetylcholine sensor for monitoring in vivo cholinergic activity. Nat Methods. 2020 Nov;17(11):1139-1146. doi: 10.1038/s41592-020-0953-2. Epub 2020 Sep 28. PMID: 32989318; PMCID: PMC7606762.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2024 Abstract

Case Study Abstract 24-03

Title: A Case OF Conversion Disorder Presenting With Blepharospasm And Hyperesthesia.

Presenting Author: Vaibhav Oberoi, PGY-1, Government Medical College and Hospital, Amritsar, India

Additional Author(s): Harini Gali M.B.B.S., Sree Balaji Medical College and Hospital, Chennai, India

Anureet Kaur Sekhon M.B.B.S., Akron General Hospital, Akron, Ohio, USA

Ashish Sarangi M.D., University of Missouri-Columbia, Columbia, MO, USA

Introduction/Background: Conversion disorder, also known as functional neurological symptom disorder, is characterized by involuntary neurologic symptoms such as paralysis, weakness, and sensory disturbances that cannot be fully explained by other medical conditions. It often presents with a calm demeanor towards the symptoms, known as "la belle indifference." This report explores a case of Conversion disorder presenting with Blepharospasm and hyperesthesia.

Description: A woman in her late 40s, a known case of controlled migraine with left-sided headaches accompanied by flashing lights and nausea but no vomiting or sleep disturbances reported to the outpatient department with sudden inability to open her left eyelid and hyperesthesia over the left eyelid. Neurological examinations and imaging, including 3D MRI, CT angiography of brain and blood tests including Acetylcholine Receptor Antibodies, were unremarkable except for low vitamin B-12 and vitamin D levels. Despite a trial of Pregabalin and Benztropine, she reported continued inability to open her left eyelid and hyperesthesia. A placebo trial in place of supratrochlear nerve block, along with motivation to open the eyelid, led to significant symptom improvement. A psychiatric evaluation revealed underlying emotional distress related to a recent conflict with her daughter, though she did not meet the criteria for clinical depression. The patient was diagnosed with Conversion disorder and began behavioral and psychotherapy.

Discussion and Conclusion: The DSM-5 diagnostic criteria for Conversion disorder include the presence of one or more neurological symptoms that cannot be better explained by another medical disorder and that cause significant distress or psychosocial impairment. The patient's presentation of Blepharospasm and hyperesthesia, despite normal neurological findings and lack of response to conventional treatments, suggested a psychogenic component. The significant improvement following the placebo trial highlighted the role of psychological factors in her symptoms. This case underscores the importance of considering psychosocial factors when diagnosing and treating neurological symptoms that may have a psychogenic origin. Early recognition of Conversion disorder can lead to more effective management, reducing patient stress and improving outcomes while optimizing resource use.

References: . Galli S, Tatu L, Bogousslavsky J, Aybek S. Conversion, FactitiousDisorder and Malingering: A Distinct Pattern or a Continuum? FrontNeurol Neurosci. 2018;42:72--80. doi:10.1159/000475699.2. Gokarakonda SB, Kumar N. La Belle Indifference. Treasure Island(FL): StatPearls Publishing; 2024.3. Marjama J, Tröster AI, Koller WC. Psychogenic movement disorders.Neurol Clin. 1995;13(2):283--97.4. First MB, Clarke DE, Yousif L, Eng AM, Gogtay N,

Appelbaum PS,et al. DSM-5-TR : Rationale, Process, and Overview of Changes.Psychiatric Services. 2023;74(8):869--75.5. Hassell TJW, Charles D. Treatment of Blepharospasm andOromandibular Dystonia with Botulinum Toxins. Toxins (Basel).2020;12(4):269. doi:10.3390/toxins12040269.6. Hallett M. Blepharospasm: recent advances. Neurology.2002;59(9):1306--12.7. Pariseau B, Worley MW, Anderson RL. Myectomy for blepharospasm2013. Curr Opin Ophthalmol. 2013;24(5):488--93.8. Hamm AR. Identification and initial treatment of involuntarypsychogenic movement (conversion) disorder in a 25-year-old malepatient. Clin Case Rep. 2021;9(10):4978. doi:10.1002/ccr3.4978.9. Inada T, Yagi G. Current topics in neuroleptic-induced extrapyramidalsymptoms in Japan. Keio J Med. 1996;45(2):95--9.10. Das S, Sreedharan RP, Remadevi PS, Saji CV. PsychogenicBlepharospasm: A Diagnostic Dilemma. Shanghai Arch Psychiatry.2016;28(6):346--8.11. Factor SA, Podskalny GD, Molho ES. Psychogenic movementdisorders: frequency, clinical profile, and characteristics. J NeurolNeurosurg Psychiatry. 1995;59(4):406--12.12. Marjama J, Tröster AI, Koller WC. Psychogenic movement disorders.Neurol Clin. 1995;13(2):283--97.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2024 Abstract

Case Study Abstract 24-04

Title: LRP4 Antibody Positive Myasthenia Gravis

Presenting Author: Dustin Casper, OMS-3, Edward via College of Osteopathic Medicine

Additional Author(s): Whitt Harrelson MS III, Dr. Naomi Thelusma MD, and Dr. Jitesh Kar, MD, MPH

Introduction/Background: To report a rare case of low-density lipoprotein receptor-4 (LRP4) antibody positive Myasthenia Gravis (MG).

Description: 53-year-old female presented with the chief complaint of fatigue and cough which began 1 year prior to arrival to clinic, gradual in onset. The symptoms worsen throughout the day worse at the end of the day. She endorsed bilateral drooping eyelids even though she had surgery to fix them. Examination showed fatigable weakness in proximal muscles mainly deltoid and mild ptosis. Initial lab work included acetylcholine receptor binding, blocking, and modulating antibodies, skeletal muscle antibodies, and striated muscle antibodies which all came back negative. Imaging studies including MRI of brain and cervical spine did not show any abnormality. She underwent NCS/EMG with repetitive nerve study, which was reported to be normal, no evidence of electrodecremental response. With the presenting symptoms of fatigue, worse as day progresses and negative serology testing, she was referred to University of Kansas neurology clinic for newer antibodies testing. Antibodies to LRP4 were tested and came back positive resulting in the diagnosis of Myasthenia Gravis. The patient is now doing well receiving IVIG every four weeks and steroids, which was eventually tapered off due to multiple side effects. She is also on pyridostigmine which is helping her symptoms.

Discussion and Conclusion: This case presents a case of Myasthenia Gravis with antibodies to LRP4 which is rarely seen with this disease. Serum testing of LRP4 or newer antibodies should be considered in patients who presents with NMJ disorder type symptoms and initial work up shows possible seronegative MG as LRP4 antibodies are up to 92% sensitive to MG.

ALABAMA ACADEMY OF NEUROLOGY

AAN 2024 Abstract

Case Study Abstract 24-05

Title: Risk for Intracranial Hemorrhage in Patients Taking Lecanemab

Presenting Author: Whitt Harrelson, MS-3, UAB Heersink School of Medicine

Additional Author(s): Whitt M. Harrelson B.S., Dustin T. Casper OMS 3, Naomi Thelusma MD, Jitesh Kar, MD, MPH

Introduction/Background: The objective of this case discussion is to highlight the increased risks for acute related imaging abnormalities (ARIA-E) with edema and acute related imaging abnormalities with hemorrhage (ARIA-H) while taking the medication Lecanbemab-irmb.

Alzheimer's disease is the most common cause of dementia worldwide, clinically characterized by short-term memory impairment, language difficulties, temporal and spatial disorientation, and deficits in executive function and judgment. Alzheimer's is due to the accumulation of extra-neuronal β-amyloid plaques and intraneuronal tau protein neurofibrillary tangles. Lecanemab is a recombinant humanized immunoglobulin gamma 1 (IgG1) anti-amyloid monoclonal antibody that binds to amyloid oligomers, protofibrils, and insoluble fibrils. It is administered as an infusion every two weeks without requiring titration at the onset of treatment. Lecanemab is most beneficial for patients with a confirmed beta amyloid pathology which is confirmed via positron emission tomography or cerebrospinal fluid tests which indicate Alzheimer's disease.

Description: 75-year-old male diagnosed with Alzheimer's in March of 2024 and confirmed by spinal tap and identification of β-amyloid in CSF. At this time, he had not completed APOE4 screening but later learned that he was heterozygous for the APOE-4 gene. After detailed discussion of risk for ARIA with patient and wife, he agreed to begin Lecanemab infusions and had his first infusion on April 24th. Patient continued treatment every other week and went for an MRI between his 4th and 5th infusions. When MRI was read, the patient was instructed to promptly go to the emergency department. At this time the patient was experiencing new onset memory decline, confusion, navigation difficulty, and was described by wife as 'almost in full blown dementia'. On 6/14 was admitted to the neuro ICU for findings of ARIA-H/E. While hospitalized, the patient received Decadron and was discharged the next day. Subsequent MRIs on June 21, July 5, July 12, and July 26, 2024, showed no worsening of edema or hemorrhage. At his initial follow up appointment (6/24) the patient had clinically worsened with further memory loss, frontal lobe headaches, confusion, dizziness, and emotional instability. Patient was subsequently started on 4mg of Dexamethasone with a dosage increase on 7/24 due to further worsening of symptoms. Imaging showed no worsening of hemorrhage and edema and patient tapered down his dose of steroids. Patient's symptoms improved over the next two weeks however, due to his prolonged period of delirium and cognitive decline it is unlikely that he will return to previous baseline.

Discussion and Conclusion: Lecanemab has appears to be beneficial for patients with a diagnosis of Alzheimer's disease, however it has shown an increasing risk of both ARIA-H and ARIA-E with the least risk associated in APOE-4 non-carriers and the most risk in APOE-4 homozygous individuals. Assessment of patient's risk factors including medication review, APOE-4 genotyping, presence of uncontrolled immunological disorder, and clotting disorders should be conducted thoroughly before

initiation of treatment. Screening and early detection of ARIA should be performed through monthly non-contrast MRI scans and clinical assessment of the patient.

References: Cummings J, Apostolova L, Rabinovici GD, Atri A, Aisen P, Greenberg S, Hendrix S, Selkoe D, Weiner M, Petersen RC, Salloway S. Lecanemab: Appropriate Use Recommendations. J Prev Alzheimers Dis. 2023;10(3):362-377. doi: 10.14283/jpad.2023.30. PMID: 37357276; PMCID: PMC10313141.

Knapskog AB, Engedal K, Selbæk G, Øksengård AR. Alzheimers sykdom -- diagnostikk og behandling [Alzheimer's disease -- diagnosis and treatment]. Tidsskr Nor Laegeforen. 2021 Apr 29;141(7). Norwegian. doi: 10.4045/tidsskr.20.0919. PMID: 33950641.