2022 Summer Conference Abstracts

Following are the Summer Conference abstracts that were presented as part of the 2022 AAN Summer Conference in San Francisco, CA, on July 15–16, 2022. Abstracts were selected based on scientific merit, breadth of audience interest, and quality of presentation.

The Prevalence and Clinical Phenotype of Dual Positive Neuromyelitis Optica Spectrum Disorders (NMOSD) at a National Reference Centre

Chirag Lalwani, Fida Faisal, Anjali Yadav, Sudheeran Kannoth, Vivek Nambiar, Sibi Gopinath, Anand Kumar, Udit Saraf, Jino Vincent, Sruthi Anoop, Annamma Mathai, Suprabha Panicker

Objective

To assess the prevalence of dual positive NMOSD and outline its clinical phenotype.

Background

Neuromyelitis Optica Spectrum Disorders (NMOSD) is an autoimmune syndrome that is frequently positive for Aquaporin 4 (AQP4) IgG or Myelin Oligodendrocyte Glycoproteins (MOG) IgG. However, dual positivity to both is rare.

Design/Methods

This is a retrospective cross-sectional study conducted at a tertiary healthcare center in South Asia between August 2018 and November 2021. The serum and/or CSF samples of suspected cases of NMOSD were tested for both AQP4-IgG and MOG-IgG using an Indirect immunofluorescence test on transfected cells.

Results

During the study period, 1935 cases of NMOSD were tested for both antibodies- 65 patients (3.36%; 57 females and 8 males) tested positive for AQP4-IgG, 217 patients (11.23%; 122 females and 95 males) tested positive for MOG-IgG and 3 patients (0.15%; 2 females and 1 male) showed dual positivity. There was a strong female preponderance in all three groups (87.69%, 56.22% and 66.66% respectively). This study identified 3 patients with dual positivity. The first patient (42 years, Male) presented with area postrema syndrome initially and subsequently relapsed by developing right-sided numbness of the temporal area and limbs during which he tested dual positive. The second patient (27 years, Female) presented with bilateral optic neuritis (left >right) initially and subsequently relapsed following an episode of a seizure with left-sided hemiplegia and right-sided facial deviation. The third patient (25 years, Female) initially presented with acute bilateral optic neuritis and later developed left-sided hemiplegia post-recovery at which point she tested dual positive. Management using methylprednisolone was ineffective for all three patients, however, plasmapheresis and/or periodic rituximab injections produced an excellent response.

Conclusions

Our study reports that the prevalence of dual positive NMOSD is 0.15% and its clinical phenotype is more similar to NMO rather than MOG-associated disease.

Disclosure: Mr. Lalwani has nothing to disclose. Miss Faisal has nothing to disclose. Anjali Yadav has nothing to disclose. The institution of Dr. Kannoth has received research support from Novartiz. Dr. Nambiar has nothing to disclose. Sibi Gopinath has nothing to disclose. Dr. Kumar has nothing to disclose. Dr. Saraf has nothing to disclose. Dr. Vincent has nothing to disclose. Ms. Sasikumar has nothing to disclose. Dr. Mathai has nothing to disclose. Mrs. Panicker has nothing to disclose.

Upregulated Complement Receptors Correlate With Fc Gamma Receptor 3A-Positive Natural Killer Cells (NK) and Natural Killer-T Cells (NKT) in Neuromyelitis Optica Spectrum Disorder

Shuhei Nishiyama, Amy Wright, Itay Lotan, Friedemann Paul, Michael Levy

Objective

To clarify if NK and NKT cells are activated via complement in NMOSD.

Background

Inhibition of terminal complement in NMOSD using eculizumab has been shown to be helpful in preventing relapses but exactly how the drug is working is not clear. Similarly, genetic variants in the Fc Gamma receptor 3A are correlated with outcomes in NMOSD but the immune cells expressing those FcGR3A receptors are unknown. We compared FcGR3A expression on immune cells modulated by complement activity in NK cells and NKT cells in NMOSD to disease controls and healthy people.

Design/Methods

Peripheral blood cell (PBMC) samples from 45 patients with NMOSD with AQP4-IgG, 18 disease controls, and 19 normal controls were analyzed for FcGR3A expression and complement receptors in vitro.

Results

At baseline, the number of NKT cells were increased in NMOSD ($p < 0.001$), but the proportion that were FcGR3A positive was lower compared to healthy and disease controls ($p = 0.0012$). NK cell count was normal at baseline but also but the proportion that were FcGR3A positive was also relatively lower ($p < 0.001$). In both NK cells and NKT cells from NMOSD, C5 complement receptor expression was much higher compared to healthy and disease controls ($p < 0.001$ for both). We also evaluated activation markers CD69 and CD83, which were also much higher in NK and NKT cells from NMOSD patients.

Conclusions

Our results support a model of immunopathogenesis model in which complement pathway activation in NK/NKT cells upregulate FcGR3A expression that bind to antibody/antigen complexes. In the context of NMOSD, these complement-sensitive cells may be responsible for escalating autoimmune activity.

Disclosure: Dr. Nishiyama has nothing to disclose. Ms. Wright has nothing to disclose. Dr. Lotan has nothing to disclose. The institution of Dr. Paul has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Mitsubishi Tanabe PC (MTPC). The institution of Dr. Paul has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Aarhus University. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Paul has received personal compensation in the range of $0-$499 for serving on a Scientific Advisory or Data Safety Monitoring board for Sanofi Genzyme. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for UCB Pharma. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for CELGENE. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Bayer. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Novartis. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for ACRELION. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Viela Bio. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Alexion. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a

Speakers Bureau for Roche. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Pfizter. Dr. Paul has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Merck Serono. The institution of Dr. Paul has received personal compensation in the range of $500-$4,999 for serving as an Editor, Associate Editor, or Editorial Advisory Board Member for Springer. Dr. Levy has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Mitsubishi Pharma. Dr. Levy has received personal compensation in the range of $500-$4,999 for serving as a Consultant for UCB Pharma. Dr. Levy has received personal compensation in the range of $5,000-$9,999 for serving as a Consultant for Sanofi. Dr. Levy has received personal compensation in the range of $5,000-$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Levy has received personal compensation in the range of $5,000-$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Horizon. Dr. Levy has received personal compensation in the range of $5,000-$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Levy has received personal compensation in the range of $500-$4,999 for serving as an Editor, Associate Editor, or Editorial Advisory Board Member for Elsevier. Dr. Levy has received personal compensation in the range of $10,000-$49,999 for serving as an Expert Witness for Various law firms. The institution of Dr. Levy has received research support from National Institutes Health.

FDA Approved Treatments for Neuromyelitis Optica Spectrum Disorder in Clinical Practice: A Survey of Academic Neuroimmunologists

Jesse Thon, Robert Sharkus, Richa Thakkar, Krystal Hunter, James Siegler, Olga Thon

Objective

To assess utilization and barriers to use of three recently FDA-approved treatments for neuromyelitis optica spectrum disorder (NMOSD) by academic neuroimmunologists.

Background

Since 2019, eculizumab, inebilizumab, and satralizumab have received FDA approval for the treatment of aquaporin-4 IgG positive (AQP4+) NMOSD after showing efficacy in reducing attack frequency. However, little is known regarding the adoption of these therapies into practice or barriers to their use. We conducted a survey of academic neuroimmunologists to identify current treatment practices.

Design/Methods

An electronic survey study was conducted of US neuroimmunologists. Recipients were identified on department websites of university-associated hospitals with affiliated neurology residencies. The survey was administered via email, and included questions regarding clinical background, patient cohort, treatment use in different scenarios, and barriers. The authors were blinded to the identity of respondents.

Results

383 neuroimmunologists from 105 institutions were identified, of whom 33 from 18 states completed the survey. Nearly all (88%) reported treating patients with the newly FDA-approved therapies (NFTs). None reported discomfort discussing any NFT with their patients. Respondents reported uncommonly switching clinically stable patients to NFTs (69% never switch, 22% switch 1-25% of the time). For newly diagnosed AQP4+ NMOSD patients, NFT initiation rates varied (16% initiate none, 42% 1-25% of the time, 6.5% 25-50%, 19% 50-75%, 16% 75-100%). For patients with a relapse, responses were dichotomized regarding switching to NFTs - respondents either switch 75-100% of their patients (60%) or none or 1-25% (16%, 24% respectively). Nearly half (16/33) of respondents reported being unable to start NFTs, with insurance/cost issues being the most cited barrier.

Conclusions

Among academic neuroimmunologists, FDA-approved therapies for AQP4+ NMOSD are being utilized for newly diagnosed patients and those with disease recurrence, although individual practice patterns vary. The main perceived barriers to NFT use are insurance/cost-related issues.

Disclosure: An immediate family member of Dr. Thon has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Horizon. An immediate family member of Dr. Thon has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Genentech. An immediate family member of Dr. Thon has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Genentech. Dr. Thon has received personal compensation in the range of $500-$4,999 for serving as a Focus group participant with Alexion. Dr. Sharkus has nothing to disclose. Dr. Thakkar has nothing to disclose. Krystal Hunter has nothing to disclose. Dr. Siegler has received personal compensation in the range of $10,000-$49,999 for serving as a Consultant for Ceribell. Olga Thon has nothing to disclose.

Safety and Effectiveness of Eculizumab in Japanese Patients With Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder: Interim Analysis of a Post-marketing Surveillance Study

Ichiro Nakashima, Yo Hoshino, Kazumi Okamura, Hidekazu Kikui, Kazuo Fujihara, Yuriy Edwards

Objective

NA.

Background

The terminal complement C5 inhibitor eculizumab is approved in Japan for the prevention of aquaporin-4 antibody-positive (AQP4+) neuromyelitis optica spectrum disorder (NMOSD) relapse and undergoing mandatory post-marketing surveillance (PMS) of real-world use.

Design/Methods

This PMS interim analysis assessed eculizumab's safety and effectiveness in Japanese patients AQP4+ NMOSD patients from approval (November 2019) to interim data cut-off (1 April 2021).

Results

At data cut-off, 79 patients treated with eculizumab were registered under PMS. Data were available for 20 patients who provided consent for publication and constituted the safety data set; three patients from the phase 3 PREVENT study were excluded from the effectiveness data set. Two patients discontinued before data cut-off owing to physician or patient decision (one each). In the effectiveness data set, 16/17 (94%) patients were female, mean illness duration was 9.2 years (standard deviation [SD] 7.5 years, range 0.3–23.8 years) and mean age at eculizumab initiation was 48.6 years (SD 11.9 years, range 27–77 years). In the 2 years before eculizumab, 12/17 patients experienced relapse, and 6/17 experienced =2 relapses. Importantly, no relapses were reported in the effectiveness data set (10.7 patient-years [PY] of treatment); this compared favorably with a 0.65/PY relapse rate in the 2 years before treatment (34.0 PY). Three adverse events (malaise, eyelid oedema, erythema) and one serious adverse event (urinary tract infection [UTI]) were observed in three patients in the safety data set: eyelid oedema and erythema (one patient) were deemed treatment-related; malaise and UTI were deemed unrelated to treatment. No meningococcal infections were reported, and the safety results were consistent with those from PREVENT.

Conclusions

For the first time in a real-world setting, eculizumab was effective in preventing relapses and well tolerated in Japanese patients with AQP4+ NMOSD, consistent with its efficacy and safety profile in the global phase 3 PREVENT study.

Disclosure: Dr. Nakashima has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Nakashima has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board