Design/Methods

This study was performed at the Mayo Clinic Neuroimmunology Laboratory. The ANNA3-IgG antigen, identified by immunoprecipitation and mass spectrometry as Dachshund-homolog 1 (DACH1), was confirmed by using a commercial DACH1-specific IgG for immunohistochemical colocalization, antigen-specific Western blot, transfected cell-based immunofluorescence, and immune absorption experiments. Clinical data were abstracted from patients' medical records or provided by referring physicians.

Results

IgG in 32 ANNA3 seropositive patient sera, but in none of 145 controls, bound to DACH1. Clinical information was available for 30 patients (median age, 63.5 years [range, 49-88]; 67% female). Neurological manifestations included neuropathy, 12; cognitive difficulties or encephalitis, 11; ataxia, 8; dysautonomia, 7 (two additionally had diarrhea and esophageal spasm); chorioretinopathy, 1. Clinical improvement was noted in 8 of 11, all treated with immunosuppressants or oncologic treatment. In two patients, the neurological syndrome appeared or worsened during immune checkpoint inhibitor cancer immunotherapy. A neoplasm was found in 27 patients (90%); fourteen were of neuroendocrine lineage. Coexisting neural autoantibodies were detected in 14 patients (47%), and most predicted a neuroendocrine tumor (specific for neuronal intermediate filaments, collapsin response-mediator protein-5, voltage-gated calcium channel [P/Q-type], ANNA1, SOX1, Purkinje-cell cytoplasmic autoantibody type 2/microtubule-associated-protein-1B).

Conclusions

IgG specific for DACH1 is a serological biomarker of neurological autoimmunity and cancer in patients of middle-age or older. DACH1-IgG is a valuable addition to comprehensive autoimmune and paraneoplastic neural antibody evaluations in clinical practice.

Disclosure: The institution of Dr. Zekeridou has received research support from Roche/Genentech. Dr. Zekeridou has received intellectual property interests from a discovery or technology relating to health care. Dr. Zekeridou has received intellectual property interests from a discovery or technology relating to health care. Ms. Yang has nothing to disclose. The institution of Dr. Lennon has received research support from NIH. Dr. Lennon has received intellectual property interests from a discovery or technology relating to health care. The institution of Dr. Lennon has received research support from NIH. Dr. Lennon has received intellectual property interests from a discovery or technology relating to health care. Guo Yong has nothing to disclose. Dr. Wu has nothing to disclose. Dr. Lucchinetti has received personal compensation in the range of $500-$4,999 for serving as an officer or member of the Board of Directors for Mayo Clinic. The institution of Dr. Lucchinetti has received research support from Biogen Idec. The institution of Dr. Lucchinetti has received research support from NIH/NINDS. The institution of Dr. Lucchinetti has received research support from National Institute of Neurological Disorders and Stroke. The institution of Dr. Lucchinetti has received research support from National Multiple Sclerosis Society. Dr. Lucchinetti has received intellectual property interests from a discovery or technology relating to health care. Dr. Lucchinetti has a non-compensated relationship as a Member with National Institute of Neurological Disorders that is relevant to AAN interests or activities. Dr. Lucchinetti has a non-compensated relationship as a Member with American Neurological Association Board of Directors that is relevant to AAN interests or activities. Dr. Lucchinetti has a non-compensated relationship as a Member with Board of Directors, Association of University Professors of Neurology that is relevant to AAN interests or activities. Dr. Lucchinetti has a non-compensated relationship as a Member with Mayo Clinic Board of Trustees that is relevant to AAN interests or activities. The institution of Dr. McKeon has received research support from Euroimmun AG. The institution of Dr. McKeon has received research support from National Institutes of Health. Dr. McKeon has received intellectual property interests from a discovery or technology relating to health care. Dr. McKeon has received intellectual property interests from a discovery or technology relating to health care. Dr. McKeon has received publishing royalties from a publication relating to health care. Dr. Pittock has received personal compensation in the range of $5,000-$9,999 for serving as a Consultant for Genentech, Inc. Dr. Pittock has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Sage Therapeutics, Inc. The institution of Dr. Pittock has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Astellas. Dr. Pittock has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Prime Therapeutics. Dr. Pittock has received personal compensation in the range of $500-$4,999 for serving as a Consultant for UCB. Dr. Pittock has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Roche/Genentech. The institution of Dr. Pittock has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Alexion. The institution of Dr. Pittock has received personal compensation in the range of $500-$4,999 for serving as a Consultant for MedImmune/Viela Bio. Dr. Pittock has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for UCB, Inc. Dr. Pittock has received personal compensation in the range of $5,000-$9,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Hoffman/LaRoche AG. Dr. Pittock has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genetech. Dr. Pittock has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for F. Hofman/LaRoche. The institution of Dr. Pittock 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. The institution of Dr. Pittock has received research support from Grifols. The institution of Dr. Pittock has received research support from NIH. The institution of Dr. Pittock has received research support from Viela Bio/MedImmune/Horizon. The institution of Dr. Pittock has received research support from Alexion Pharmaceuticals. The institution of Dr. Pittock has received research support from F. Hoffman/LaRoche/Genentech. Dr. Pittock has received intellectual property interests from a discovery or technology relating to health care. Dr. Pittock has received intellectual property interests from a discovery or technology relating to health care. The institution of Dr. Flanagan 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. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Horizon Therapeutics. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Pharmacy times. The institution of Dr. Flanagan has received research support from Viela Bio. Dr. Flanagan has a non-compensated relationship as a Member of medical Advisory Board with The MOG Project that is relevant to AAN interests or activities. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Journal of The Neurologic Sciences that is relevant to AAN interests or activities. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Neuroimmunology Reports that is relevant to AAN interests or activities.

Examining the Differences in Biomarkers of Neuronal and Glial Injury Between Autoimmune Neurologic Disease Patients and Healthy Controls

Tyler L. Borko, Britney Barrera, Christopher Mizenko, Aurélie Ledreux, Ryan Kammeyer, Alanna Ritchie, Sean Selva, Stefan Sillau, Eric Engebretson, Rebecca Seale, Brooke Valdez, Jeffrey L. Bennett, Timothy L. Vollmer, Kavita Nair, Amanda Piquet

Objective

To evaluate differences in concentrations of serum-based biomarkers obtained from a screened healthy control (HC) population compared to age and sex matched autoimmune and inflammatory neurologic disease (AIND) patients.

Background

Protein markers of neuronal and glial injury have become important, minimally invasive biomarkers for understanding the impact of disease in various neurological disorders, including ongoing research into AINDs. Levels of these proteins in healthy individuals remain unclear.

Design/Methods

Neurofilament light (NfL), glial fibrillary acidic protein (GFAP), ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1), and total tau (Tau) levels in AIND and HC participants will be compared. Multiple Sclerosis (MS) patients, as inflammatory controls, will be analyzed as

well. AIND and HC participant serum samples have been collected to obtain NfL, GFAP, UCH-L1, and Tau protein levels using Quanterix SR-XTM SIMOA. We plan to analyze and compare age and sex matched HC samples to AIND patients for each biomarker, ages ranging from 20-80 years old. Concentrations will be log transformed and analyzed with mixed model regression.

Results

Healthy Controls (130), AIND (255), and newly diagnosed/treatment naïve MS samples (681) have already been collected. Nineteen HC and AIND (includes NMDA, LGI1, TRIM46, CRMP5, MOG, DPPX, GABA-A, GAD-65) participants were analyzed. Preliminary results for HC show mean Nfl (10.3 pg/mL), GFAP (78.9 pg/mL), UCH-L1 (5.65 pg/mL), and Tau (0.53 pg/mL) levels, and for AIND patients mean Nfl (186.48 pg/mL), GFAP (434.92 pg/mL), UCH-L1 (71.38 pg/mL), and Tau (51.85 pg/mL) levels. While ongoing biomarker analysis will be completed with HC that are age and sex matched, the significantly higher levels in AIND patients highlights the importance of creating baseline values in HC to understand these same biomarkers in AIND patients.

Conclusions

Preliminary results show NfL and GFAP levels are significantly higher in AIND patients versus HC. Baseline biomarker values are essential for understanding further research in biomarkers related to AIND.

Disclosure: Mr. Borko has nothing to disclose. Ms. Barrera has nothing to disclose. Mr. Mizenko has nothing to disclose. The institution of Aurelie Ledreux has received research support from Alzheimer's Association. The institution of Dr. Kammeyer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Genentech. Mrs. Ritchie has nothing to disclose. Sean Selva has nothing to disclose. The institution of Stefan Sillau has received research support from Alzheimer's Association. The institution of Stefan Sillau has received research support from Hewitt Family Foundation; State of Colorado. The institution of Stefan Sillau has received research support from PCORI. The institution of Stefan Sillau has received research support from NINR. The institution of Stefan Sillau has received research support from Michael J. Fox Foundation. The institution of Stefan Sillau has received research support from Department of Defense. The institution of Stefan Sillau has received research support from Colorado Department of Public Health and Environment. The institution of Stefan Sillau has received research support from Benign Essential Blepharospasm Research Foundation. Stefan Sillau has a non-compensated relationship as a Statistician with Novartis that is relevant to AAN interests or activities. Stefan Sillau has a non-compensated relationship as a Statistician with Biogen that is relevant to AAN interests or activities. Mr. Engebretson has nothing to disclose. Ms. Seale has stock in Johnson & Johnson. Ms. Valdez has a non-compensated relationship as a Valdez with The Rocky Mountain MS Center non-profit partner that is relevant to AAN interests or activities. Dr. Bennett has received personal compensation in the range of $10,000-$49,999 for serving as a Consultant for Horizon Therapeutics. Dr. Bennett has received personal compensation in the range of $10,000-$49,999 for serving as a Consultant for Alexion. Dr. Bennett has received personal compensation in the range of $10,000-$49,999 for serving as a Consultant for Genentech-Roche. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving as a Consultant for TG Therapeutics. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Reistone Bio. Dr. Bennett has received personal compensation in the range of $5,000-$9,999 for serving as a Consultant for Abbvie. Dr. Bennett has received personal compensation in the range of $0-$499 for serving as a Consultant for Novartis. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Chugai. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Mitsubishi Tanabe. Dr. Bennett has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Clene Nanomedicine. Dr. Bennett 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. Bennett has received personal compensation in the range of $500-$4,999 for serving as an Expert Witness for Parker,Whiteford Taylor. Dr. Bennett has received personal compensation in the range of $5,000-$9,999 for serving as an Expert Witness for Podoll. Dr. Bennett has received personal compensation in the range of $5,000-$9,999 for serving as an Expert Witness for Hogan Lovells. The institution of Dr. Bennett has received research support from Novartis. The institution of Dr. Bennett has received research support from Alexion. Dr. Bennett has received intellectual property interests from a discovery or technology relating to health care. Dr. Bennett has received publishing royalties from a publication relating to health care. The institution of Dr. Vollmer has received personal compensation in the range of $5,000-$9,999 for serving as a Consultant for Biogen IDEC. The institution of Dr. Vollmer has received personal compensation in the range of $10,000-$49,999 for serving as a Consultant for Genentech/Roche. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Siranax. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Celgene. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for EMD Serono. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Bristol Meyers Squib. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Viela Bios. The institution of Dr. Vollmer has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Novartis. The institution of Dr. Vollmer has received research support from Rocky Mountain MS Center. The institution of Dr. Vollmer has received research support from Biogen. The institution of Dr. Vollmer has received research support from Actelion. The institution of Dr. Vollmer has received research support from Genentech/Roche. The institution of Dr. Vollmer has received research support from Anokion. The institution of Dr. Vollmer has received research support from TG Therapeutics. Dr. Nair has received personal compensation in the range of $5,000-$9,999 for serving as a Consultant for Bristol Meyers Squibb. Dr. Nair has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Novartis. Dr. Nair has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Sanofi-Genzyme. The institution of Dr. Nair has received research support from Genentech. The institution of Dr. Nair has received research support from Novartis. The institution of Dr. Nair has received research support from Genentech. The institution of Dr. Nair has received research support from Phrma Foundation. The institution of Dr. Nair has received research support from Bristol Meyers Squibb. The institution of Dr. Piquet has received personal compensation in the range of $500-$4,999 for serving as a Consultant for Genentech. Dr. Piquet has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Piquet has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. The institution of Dr. Piquet has received research support from Rocky Mountain MS Center. The institution of Dr. Piquet has received research support from Novartis. The institution of Dr. Piquet has received research support from Abbvie. The institution of Dr. Piquet has received research support from Roche/Genentech. The institution of Dr. Piquet has received research support from NYU. Dr. Piquet has received publishing royalties from a publication relating to health care. Dr. Piquet has received publishing royalties from a publication relating to health care. Dr. Piquet has received personal compensation in the range of $5,000-$9,999 for serving as a Litigative Consultant with US-Dept HHS/DICP.

A Severe Case of Lupus Cerebritis

Christopher Szewczyk, Hemil Gonzalez

Objective

Lupus cerebritis is a rare but potentially fatal complication of SLE. Prompt diagnosis and rapid initiation of therapy can prove lifesaving.

Background

We present the case of a 31-year-old woman who presented to the emergency department with one week of fevers, headaches and confusion. Review of systems was notable for diffuse muscle and joint pains, weakness and a rash. SLE and Sjogren's were both diagnosed six months prior to admission and treatment included prednisone, methotrexate, and hydroxychloroquine. She self-discontinued therapy six weeks prior to seek natural remedies in her native Ecuador. Vitals on admission were 102.2 F, 111 beats/min, 96/67 mmHg, 16 breaths/min and 95% SO2 on 2 L/min via nasal cannula. Physical exam was notable for conjunctival injection, hypopyon (OD), and oral ulcers with visible bleeding. Pelvic exam showed shallow ulcerations of the vaginal mucosa. Neurological exam was significant for diffuse weakness. There were punched-out ulcers on the digits of both hands. Laboratory markers of lupus disease

Examining the Differences in Biomarkers of Neuronal and Glial Injury Between Autoimmune Neurologic Disease Patients and Healthy Controls

Tyler L. Borko, Britney Barrera, Christopher Mizenko, et al.

Neurology 2022;99;S8-S9
DOI 10.1212/01.wnl.0000903096.36040.1d