Sendai Conference 2025

多発性硬化症および視神経脊髄炎に関する国際会議

会　期

2025. 7/5 (土) 9:00~17:00

TKPガーデンシティ仙台　〒980-6130　仙台市青葉区中央1-3-1

主　催

NPO法人日本多発性硬化症ネットワーク

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共催企業

ALEXION AstraZeneca Rare Disease / Mitsubishi Tanabe Pharma / 中外製薬 Roche グループ / NOVARTIS / Biogen

NPO法人 日本多発性硬化症ネットワーク
JAPAN MULTIPLE SCLEROSIS NETWORK

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Sendai Conference 2025

Date: 5 July, 2025
Venue: Hall 21B＋C, TKP Garden City Sendai
(AER 21F, 1-3-1 Chuo, Aobaku, Sendai)

Time Schedule

9:00～ 9:05	Opening Remarks
9:05～10:05	Oral Session 1
10:10～11:00	Sponsored Session 1 (Sponsored by Novartis Pharma K.K.)
11:00～11:10	Coffee Break
11:10～12:00	Sponsored Session 2 (Sponsored by Biogen Japan Ltd.)
12:00～12:10	General Membership Meeting of NPO
12:10～13:00	Lunch & Poster viewing
13:00～13:10	Photo Session
13:10～14:00	Sponsored Session 3 (Sponsored by Chugai Pharmaceutical Co., Ltd.)
14:00～15:00	Oral session 2
15:00～15:10	Coffee Break
15:10～16:00	Sponsored Session 4 (Sponsored by Alexion Pharma G.K.)
16:00～16:10	Coffee Break
16:10～17:00	Sponsored Session 5 (Sponsored by Mitsubishi Tanabe Pharma)
17:00	Closing Remarks (& Award ceremony)

Sendai Conference 2025 Program

9:00～ 9:05 Opening Remarks

OR Dr. Kazuo Fujihara

9:05～10:05 Oral session 1 (Chair: Dr. Jin Nakahara & Dr. Tomoko Okamoto)

OS1-1 Dr. Kimihiko Kaneko (Tohoku University)
Temporal change in the treatment of MS and NMOSD with novel DMD in Tohoku University over the past 5 years

OS1-2 Dr. Naoya Yamazaki (Tohoku University)
Significance of MOG-IgA or IgM in the patients with central nervous system inflammatory disease

OS1-3 Dr. Haruhiko Motegi (Jikei University)
Beyond Iron Rim Lesions: Clinical Implications of Diffuse Iron Deposition Lesions as a Distinct Lesion Type in MS

OS1-4 Dr. Tomohiro Yata (Osaka University)
Effect of germline and somatic mutations to risk of neuromyelitis optica spectrum disorder

10:10～11:00 Sponsored Session 1 (Chair: Dr. Kimitoshi Kimura)

SS-1 Dr. Jennifer Massey (St Vincent's Hospital / UNSW School of Clinical Medicine)
MS Management: Preventing disease progression
(Sponsored by Novartis Pharma K.K.)

11:00～11:10 Coffee Break

11:10～12:00 Sponsored Session 2 (Chair: Dr. Kaori Sakuishi)

SS-2 Dr. Yang Mao-Draayer (Oklahoma Medical Research Foundation / University of Oklahoma)
Cellular, Molecular, and Microbial Mediators in Multiple Sclerosis and other Neuroinflammatory Disease
(Sponsored by Biogen Japan Ltd.)

12:00～12:10 General Membership Meeting of NPO

12:10～13:00 Lunch & Poster viewing

13:00～13:10 Photo Session

13:10～14:00 Sponsored Session 3 (Chair: Dr. Kazumasa Yokoyama)

SS-3 Dr. Benjamin M. Greenberg (The University of Texas Southwestern Medical Center, Dallas)

Current NMOSD Treatment Trends in the US: Trials, Post-Marketing Data and Case Studies of Satralizumab

(Sponsored by Chugai Pharmaceutical Co., Ltd.)

14:00～15:00 Oral session 2 (Chair: Dr. Kazumasa Yokoyama & Dr. Takayuki Kondo)

OS2-1 Dr. Itsuki Sano (Osaka University)

To explore the changes in GFAP and NfL concentrations in patients with AQP4-positive NMOSD

OS2-2 Dr. Hiroki Masuda (Chiba University)

Associations between the brain atrophy and clinical characteristics in patients with AQP4Ab+NMOSD

OS2-3 Dr. Kinya Matsuo (Yamaguchi University)

Investigation of Blood–Brain Barrier Dysfunction in Multiple Sclerosis According to Clinical Subtype and Genetic Background

OS2-4 Dr. Koji Sekiguchi (Keio University)

Efficacy and Fever-Associated Hospitalization Risk of Biologic Therapy in AQP4-IgG Positive NMOSD: A Retrospective Study

15:00～15:10 Coffee Break

15:10～16:00 Sponsored Session 4 (Chair: Dr. Yusei Miyazaki)

SS-4 Dr. Darin T. Okuda (UT Southwestern Medical Center)

Title:TBD

(Sponsored by Alexion Pharma G.K.)

16:00～16:10 Coffee Break

16:10～17:00 Sponsored Session 5 (Chair: Dr. Noriko Isobe)

SS-5 Dr. Jeffrey L. Bennett (University of Colorado)

B cell Depletion Therapy for NMOSD: From Mechanisms to Management

(Sponsored by Mitsubishi Tanabe Pharma)

17:00 Closing Remarks (& Award ceremony)

CR Dr. Ichiro Nakashima

Poster Session (Venue: Hall 21D)

P-1 Dr. Satoko Arai (Tokyo Women's Medical University)
Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease Presenting with Hydrocephalus Mimicking a Germ Cell Tumor: A Case Report

P-2 Dr. Koji Shinoda (Kyushu University)
A case of tumefactive demyelination during B cell depletion therapy by ofatumumab

P-3 Dr. Hideaki Mashimo (Teikyo University)
Selection of disease-modifying drugs for pediatric multiple sclerosis with high disease activity.

P-4 Dr. Yoshiyuki Matsuki (Tokyo Metropolitan Neurological Hospital)
A Case of Immune-Related Triple M Syndrome with Subclinical Polyneuropathy

P-5 Dr. Kazuki Ogawa (National Center Hospital / National Center of Neurology and Psychiatry)
Clinical evaluation of biologic agents used for treating neuromyelitis optica at our institution

P-6 Dr. Chihiro Namatame (Tohoku University)
Humanized-Aquaporin-4-Expressing Rat Created by Gene-Editing Technology and Its Use to Clarify the Pathology of Neuromyelitis Optica Spectrum Disorder

P-7 Dr. Teppei Komatsu (Jikei University)
Delayed Visual Improvement After Optic Neuritis in MOGAD: Case Report

P-8 Dr. Masahiro Mimori (Jikei University)
Selective Plasma Exchange Therapy for Acute-phase Treatment of Neuromyelitis Optica Spectrum Disorder: Case series

P-9 Dr. Hiroshi Kuroda (Fukushima Medical University/Southern TOHOKU Research Institute for Neuroscience)
A brain-biopsied case of autoimmune GFAP astrocytopathy

P-10 Dr. Isamu Takai (Juntendo University)
Differential Serum ACE Levels in MOG-AD and Anti–AQP4 Antibody–Positive NMOSD.

Oral Session 1

Chair: Jin Nakahara
(Department of Neurology, Keio University School of Medicine)
Tomoko Okamoto
(Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry)

OS1-1 Temporal change in the treatment of MS and NMOSD with novel DMD in Tohoku University over the past 5 years

Kimihiko Kaneko[1], Tatsuro Misu[1], Yoshiki Takai[1], Shuhei Nishiyama[1], Yuki Matsumoto[1], Hirohiko Ono[1], Hiroshi Kuroda[1,2,3], Toshiyuki Takahashi[4], Kazuo Fujihara[1,3], Masashi Aoki [1]

1. Department of Neurology, Tohoku University Graduate School of Medicine, Sendai, Japan
2. Multiple Sclerosis and Neuromyelitis Optica Center, Southern TOHOKU Research Institute for Neuroscience, Koriyama, Japan
3. Department of Multiple Sclerosis therapeutics, Fukushima Medical University, Fukushima, Japan
4. Department of Neurology, NHO Yonezawa National Hospital, Yonezawa, Japan

Background: Since 2019, new disease modifying drugs (DMD) have become available for relapse prevention in multiple sclerosis (MS) and anti-aquaporin 4 antibody-positive neuromyelitis optica spectrum disorder(NNOSD).

Method: We retrospectively surveyed the trends in the use of DMD for MS or NMOSD in the past 5 years by the analysis of medical records.

Results: In 2020, 2023 and 2025, the number of patients with MS and NMOSD seen in our hospital were as follows: MS:188→206→205, NMOSD: 75→83→94.

The mean age of MS patients was 44.2 years old. 157/205 MS patients were female and 29/205 had secondary progressive disease. Regarding DMD for MS, the number of cases treated with interferon beta (23→12→7) and fingolimod (60→53→33) gradually decreased, while the ones treated with ofatumumab (0→20→57) steadily increased. Dimethyl fumarate use remained stable (46→43→43), and the cases treated with natalizumab once increased, but then decreased (22→40→27). 25/27 cases were treated with extended interval dosing. Among them, the most recent median JCV index was 0.26 (0.11-3.79), and 15 cases were intermediate or negative (below 0.40).

The mean age of NMOSD patients was 57.6 years old, and 82/94 were female. Those who were treated with steroids monotherapy or steroid with immunosuppressant gradually decreased (44→38→32, 22→10→12, respectively). The mean dose of prednisolone who was treated with steroid monotherapy decrease (7.69→8.21→5.98㎎/day). Percentage of NMOSD patients who was treated with prednisolone over 10mg/day also decreased (28.9→18.4→9.1%). Meanwhile, those treated with C5 inhibitors (3→9→10), IL-6 inhibitors (0→11→26), and CD19 antibodies (0→6→13) increased. The number of hospitalizations for MS/NMOSD was on a downward trends (24→19→17).

Conclusion: The number of hospitalized MS/NMOSD patients has been decreasing in the past five years in line with a paradigm shift of DMD.

Oral Session 1

Chair: Jin Nakahara
(Department of Neurology, Keio University School of Medicine)
Tomoko Okamoto
(Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry)

OS1-2 Significance of MOG-IgA or IgM in the patients with central nervous system inflammatory disease

Naoya Yamazaki[1], Yuki Matsumoto[1], Naoki Yamamoto[1], Mizuki Otomo[1], Naohiro Sakamoto[1], Shu Umezawa[1], Chihiro Namatame[1], Hirohiko Ono[1], Kimihiko Kaneko[1], Yoshiki Takai[1], Shuhei Nishiyama[1], Hiroshi Kuroda[2,3], Toshiyuki Takahashi[4], Kazuo Fujihara[2,3], Tatsuro Misu[1], Masashi Aoki[1]

1. Department of Neurology, Tohoku University Graduate School of Medicine
2. Multiple Sclerosis & Neuromyelitis Optica Center, Southern TOHOKU Research Institute for Neuroscience
3. Department of Multiple Sclerosis Therapeutics, Fukushima Medical University
4. Department of Neurology, National Hospital Organization Yonezawa National Hospital

Objective: A presence of myelin oligodendrocyte glycoprotein (MOG)-IgG is required for the diagnosis of MOG antibody-associated disease (MOGAD) according to the international panel criteria of MOGAD (IPMOGAD). Although serum MOG-IgA or IgM can be detected in MOGAD and other central nervous system inflammatory diseases which are negative for MOG-IgG [MOG(-)CID], their clinical significance remains unclear.

Methods: We included patients who underwent MOG-IgG testing in both serum and cerebrospinal fluid (CSF) samples between 2021 and 2022. Among them, patients who were MOG-IgG positive (serum ≥1:128 or CSF ≥1:1) and MOG(-)CID patients (serum <1:16 and CSF <1:1) were further tested MOG-IgA and IgM. All tests were performed using a live cell-based assay (CBA) with confocal microscope, and rated independently by two raters. Association between each antibody and clinical characteristics including core clinical features of IPMOGAD was analyzed using chi-square test or t-test. Cutoffs of IgA or IgM were defined as follows: ≥1:32 for serum IgA, ≥1:64 for serum IgM, and ≥1:1 for CSF IgA and IgM.

Results: Among 124 MOG-IgG positive patients, 30.6% had MOG-IgA or IgM (serum IgA 13%, CSF IgA 12%, serum IgM 12%, CSF IgM 11%), whereas 11.5% of the 192 MOG(-)CID patients also had MOG-IgA or IgM (serum IgA 6.8%, CSF IgA 3.6%, serum IgM 6.3%, CSF IgM 2.6%). In MOG-IgG positive patients, serum IgM positivity was associated with optic neuritis (positive 9/15 vs negative 35/109, p=0.03) and CSF IgA positivity was associated with cortical encephalitis (positive 7/15 vs negative 20/109, p=0.02). Among the 22 MOG(-)CID patients with MOG-IgA or IgM, 16 (73%) had at least one core clinical demyelinating event, and of those, 14 (88%) had supportive clinical or radiological features.

Conclusions: MOG-IgA or IgM were detected in both MOG-IgG-positive and MOG(-)CID patients. Further studies are needed regarding longitudinal evaluation and significance of isolated MOG-IgA or IgM positivity.

Oral Session 1

Chair: Jin Nakahara
(Department of Neurology, Keio University School of Medicine)
Tomoko Okamoto
(Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry)

OS1-3 Beyond Iron Rim Lesions: Clinical Implications of Diffuse Iron Deposition Lesions as a Distinct Lesion Type in MS

Haruhiko Motegi, Teppei Komatsu, Hideyuki Shimizu, Hiroki Sarukawa, Motohiro Okumura, Marina Masui, Masahiro Mimori, Hiroyuki Kida, Masakazu Ozawa, Yuri Shojima, Yuki Asahara, Hiromasa Matsuno, Keiko Bono, Kenichi Sakuta, Kenichiro Sakai, Hidetaka Mitsumura, Yasuyuki Iguchi

Department of Neurology, The Jikei University School of Medicine, Tokyo, Japan

Background: Susceptibility-weighted imaging (SWI) is an MRI sequence highly sensitive to iron deposition. In multiple sclerosis (MS), iron-laden activated microglia can produce paramagnetic rim lesions (PRLs) visible on SWI, reflecting chronic active lesions. Other forms of iron-related lesions may also be present in MS but are less well characterized.

Objective: To characterize the spectrum of iron deposition lesions detectable by 3T SWI in MS patients, including established PRLs and potential novel lesion types.

Methods: We retrospectively reviewed clinical records and 3T MRI scans (including SWI sequences) from MS patients seen at our hospital between January 1, 2018 and February 28, 2025. We defined diffuse hypointense lesions on SWI that were distinct from PRLs as diffuse iron deposition lesions (dIDLs).

Results: Of 100 MS patients initially identified, 91 had complete data and were included (61 females; 78 relapsing-remitting MS [RRMS], 13 progressive MS [PMS]; mean age 44 ± 11 years; median disease duration 11 years [IQR 5–18]; median EDSS 1.0 [IQR 0–3]). Only 3 patients fulfilled the central vein sign criterion (SELECT-6, CVS ≥6 lesions). PRLs were observed in 11 patients, whereas dIDLs were detected in 39 patients. The number of dIDLs was significantly higher in PMS (median 1, IQR 0–5) than in RRMS (median 0, IQR 0–1; p=0.04).

Conclusion: Our findings suggest that routine clinical 3T SWI may be insufficient to reliably detect the central vein sign and PRLs. However, diffuse iron deposition lesions were frequently observed, particularly in PMS. These dIDLs may reflect microglial activation and iron deposition and represent a novel type of iron-related lesion distinct from PRLs.

Oral Session 1

Chair: Jin Nakahara
(Department of Neurology, Keio University School of Medicine)
Tomoko Okamoto
(Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry)

OS1-4 Effect of germline and somatic mutations to risk of neuromyelitis optica spectrum disorder

Tomohiro Yata[1,2,3], Kotaro Ogawa[1], Go Sato[2,4,5], Tatsuhiko Naito[2,5], Kyuto Sonehara[2,5,6], Ryuya Edahiro[2,5,7], Shinichi Namba[2,5,6], Mitsuru Watanabe[8], Makoto Kinoshita[1], Takuya Matsushita[8,9] Jun-ichi Kira,[8,10] Hideki Mochizuki[1] Noriko Isobe,[8] Tatsusada Okuno,[1] and Yukinori Okada[2,5,6]

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5. Laboratory for Systems Genetics, RIKEN Center for Integrative Medical Sciences
6. Department of Genome Informatics, Graduate School of Medicine, The University of Tokyo
7. Department of Respiratory Medicine and Clinical Immunology, Osaka University Graduate School of Medicine
8. Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University
9. Department of Neurology, Kochi Medical School, Kochi University
10. Translational Neuroscience Center, Graduate School of Medicine, and School of Pharmacy at Fukuoka, International University of Health and Welfare

Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease characterized by optic neuritis and transverse myelitis. Due to its low prevalence, the genetic background of NMOSD remains unclear. We conducted a genome-wide association study (GWAS) meta-analysis of NMOSD in Japanese (240 patients and 50,578 controls). We identified NMOSD risks in the major histocompatibility complex (MHC) region and *CCR6* (rs12193698; $P = 1.8 \times 10^{-8}$, odds ratio [OR] = 1.73), a novel associated gene. To elucidate the cell-type-specific expression profile of the putative target gene, we performed single-cell RNA sequencing (scRNA-seq) in peripheral blood cells from 25 NMOSD patients and 101 controls. The risk variant at *CCR6* showed disease-specific expression quantitative trait loci effects in $CD4^+$ memory T cells, especially in T helper 17 cells. We also analyzed genotype data to detect mosaic chromosomal alterations (mCAs) at the chromosomal level, including copy number alterations (CNAs) and copy-neutral loss of heterozygosity (CN-LOH). We detected mCAs using genome data from 232 NMOSD patients, 48,394 healthy controls, 1,301 hematologic malignancy patients, and 4,384 patients with autoimmune diseases other than NMOSD. In contrast to other autoimmune diseases, NMOSD showed strong associations with both CNAs (OR = 3.37) and CN-LOH (OR = 2.18), comparable to hematologic malignancy. mCAs on chromosome 21q were specifically enriched in NMOSD. In scRNA-seq data from two NMOSD cases with 21q loss, mutated cells were enriched in $CD4^+$ T cells. These mutated $CD4^+$T cells exhibited downregulation of genes involved in type I interferon-related pathways. In this study, we obtained new insights into the pathogenesis of NMOSD from two aspects: germline and somatic mutations. We initially reported the GWAS-driven NMOSD risk outside the MHC region and the strong association between mCAs and NMOSD. By combining scRNA-seq data in both approaches, we confirmed cell-type-specific effects, especially in $CD4^+$ T cells.

Sponsored Session 1

Chair: Kimitoshi Kimura
(Department of Neurology, Kyoto University Graduate School of Medicine, Japan
Program-Specific Junior Associate Professor)

SS-1 MS Management: Preventing disease progression

Jennifer Massey MBBS (Hon) FRACP PhD

Staff Specialist Neurologist SVHNS, MS Research Australia Post-Doctorate Fellow, Senior Lecturer UNSW School of Clinical Medicine

This lecture will review the natural history of progressive MS, definitions around relapse associated worsening and progression independent of relapse activity, and patho-mechanisms of progression in MS. Dr Massey will then discuss management of progressive MS, in regards to current available disease modifying therapies, and novel advances in the field.

CURRICULUM VITAE

Dr. Jennifer Massey is a leading expert in neurology, serving as a Staff Specialist Neurologist at St Vincent's Hospital in Sydney, with a particular focus on multiple sclerosis (MS) and neuroimmunological diseases.

After graduating with honours from the University of Western Australia in 2009, Dr. Massey completed her neurology specialty training in 2018 and obtained her PhD in 2021, concentrating on immune reconstitution therapies, including autologous hematopoietic stem cell transplantation (AHSCT) for MS. Currently, Dr. Massey leads a translational research program investigating the immunopathogenesis of MS, with an emphasis on the role of viral drivers such as Epstein-Barr virus (EBV). Her innovative work includes extensive laboratory-based research in deep immunophenotyping and the application of advanced cellular therapies like CAR-T cells. As a Senior Lecturer at UNSW's School of Clinical Medicine, she is dedicated to medical education.

Dr. Massey has received grant funding from MS Australia and the NHMRC. She remains actively involved in various clinical trials and research initiatives aimed at improving patient outcomes in MS. She has attended national and international conferences, where she presents her findings on immune reconstitution therapies and the complexities of MS treatment.

Passionate about patient care, Dr. Massey integrates her clinical practice with her research, pushing for innovative solutions to enhance the lives of individuals with MS.

Chair: Kaori Sakuishi
(Department of Neurology, Teikyo University Chiba Medical Center)

SS-2 Cellular, Molecular, and Microbial Mediators in Multiple Sclerosis and other Neuroinflammatory Disease

Yang Mao-Draayer, MD, PhD

Professor in Neurology, Director of Clinical and Experimental Therapeutics,
Multiple Sclerosis Center of Excellence, Autoimmunity Center of Excellence,
Arthritis and Clinical Immunology Research Program,
Oklahoma Medical Research Foundation
Professor in Pathology, Professor in Microbiology and Immunology,
University of Oklahoma, College of Medicine

Talk abstract:

Dr. Yang Mao-Draayer's presentation will review her research on molecular, cellular and microbial mediators for neuroimmune and treatment responses and identification of promising biomarkers that distinguish various forms of MS and other neuroinflammatory diseases.

1. Comprehensive deep immunophenotyping of T, B lymphocytes as well as innate immune cells with various DMTs in MS.
2. Discovery of T cell costimulatory molecule sCD40L as a predictive biomarker for MS disease progression and therapeutic development of humanized monoclonal antibody to CD40L in MS.
3. Metabolites and microbiome work demonstrating short-chain fatty acid (SCFA) and unique gut microbiome links disease progression in MS.
4. Multiplexed proteomic and transcriptomics to identify protein signatures associated with disease in NMOSD subtype including AQP4+NMOSD, MOG+NMOSD and serum negative NMOSD.

CURRICULUM VITAE

Dr. Yang Mao-Draayer is a Professor and Director of Clinical and Experimental Therapeutics at the Oklahoma Medical Research Foundation. She has authored over 100 peer-reviewed research articles and >100 abstracts. She has served in many national and international study sections, including NIH, DOD, NMSS, and FDA. She has served on the National Healthcare Advisory Committee for the National Multiple Sclerosis Society. She was also named the chair of the Health and Economic Committee for the North American Registry for Care and Research in MS (NARCRMS). In addition, she has been an elected member of the Neuromyelitis Optica (NMO) Guthy Jackson Charitable Foundation International Clinical Consortium and Biorepository (ICCB) among a total of 80 ICCB members worldwide since 2015.

She has been a neurologist and physician scientist specializing in Multiple Sclerosis and Neuromyelitis Optica since 2005. She completed both MD and PhD degrees, the latter degree in Biology and Molecular Genetics from the University of Iowa. She completed neurology residency and Neuroimmunology fellowship training at the University of Vermont, where she served as chief resident. In 2012 she was recruited to the University of Michigan to build MS human immunology research program and was promoted to be full Professor in 2018.

She has served as the Director of Neuroscience Research of the Autoimmune Center of Excellence (ACE) funded by National Institute of Health (NIH/NIAID) since 2014. She has successfully assembled an ACE multi-centered collaborative groups with 15 US MS centers and served as protocol chair and primary project Principal Investigator (PI) leading the central lab of the ACE. Her lab pursues bench-to-bedside-and-back translational and clinical studies in MS. Her ACE study provided immunological and molecular insights for MS disease progression. Her group has provided mechanistic understanding of immune cell changes with many disease modifying therapies in MS. Her group was the first to report deep immunophenotyping of T and B cells with dimethyl fumarate in MS (IJMS 2015; Neurol N2 2016; JI 2017; Front Neurol 2018); which was validated by Biogen in a larger multi-centered study (MSJ 2020). Her recent work led to the discovery of T cell costimulatory molecule sCD40L as a predictive biomarker for MS disease progression. She published investigator-initiated phase I study using humanized monoclonal antibody to CD40L in MS, which led to success phase II data on published in NEJM. In addition, her group also studied body metabolites and discovered bimodal regulatory effects of short-chain fatty acid (SCFA) which links disease progression in MS. Her recent work showed that MS disease progressors exhibit a unique baseline gut microbial signature. Furthermore, her collaborative group also identified protein signatures associated with disease in NMOSD subtype including AQP4+NMOSD, MOG+NMOSD and serum negative NMOSD.

Chair: Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)

SS-3 Current NMOSD Treatment Trends in the US: Trials, Post-Marketing Data and Case Studies of Satralizumab

Benjamin Greenberg

Professor, Neurology The University of Texas Southwestern Medical Center

With the availability of 4 approved therapies for AQP4 seropositive neuromyelitis optica in the United States patients have a multitude of options for preventing relapses. While there are no head-to-head trials comparing the various medications, there is a lot of clinical trial and post marketing data and experience that can be used to classify these therapies. The medications vary in route of administration, frequency of administration, mechanism of action and relative risk of complications. Additionally, some interventions can impact vaccine efficacy or require prophylaxis for infectious complications. This presentation will briefly review the clinical trial data for the available therapies, but then focus on real world data about efficacy and risk. Post marketing data will be used to identify trends in prescribing, considerations for dual therapy and practical barriers to utilization. Case studies will be used to explore patient medical history or demographic characteristics that may impact therapy selection.

CURRICULUM VITAE

Dr. Benjamin Greenberg received his Bachelor of Arts degree from Johns Hopkins University and his Masters Degree in Molecular Microbiology and Immunology from the Johns Hopkins School of Public Health in Baltimore, Maryland. He attended medical school at Baylor College of Medicine in Houston, Texas. He completed his residency in neurology at The Johns Hopkins Hospital in Baltimore, MD. He then joined the faculty within the division of neuroimmunology at Johns Hopkins and became the co-director of the Transverse Myelitis Center. In January of 2009 he was recruited to the faculty at the University of Texas Southwestern Medical Center where he founded the new Transverse Myelitis and Neuromyelitis Optica Program.

Dr. Greenberg is focused on rare autoimmune disorders of the central nervous system (e.g. transverse myelitis, neuromyelitis optica, ADEM and autoimmune encephalitis). His research interests are in both the diagnosis and treatment of transverse myelitis, neuromyelitis optica, encephalitis and multiples sclerosis. He is actively involved in developing better ways to diagnose and prognosticate for patients with these disorders. His research has identified novel biomarkers that may be able to distinguish between patients with various neurologic disorders. He also coordinates trials that study new treatments to prevent neurologic damage and restore function to those who have already been affected. He currently serves as Vice Chair of Clinical and Translational Research for the Department of Neurology at the University of Texas Southwestern.

Oral Session 2

Chair: Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)
Takayuki Kondo
(Kansai Medical University Medical Center)

OS2-1 To explore the changes in GFAP and NfL concentrations in patients with AQP4-positive NMOSD

Itsuki Sano, MD, Naoshi Koizumi, MD, Ryohei Yamamura, MD, Toru Koda, MD, PhD,
Makoto Kinoshita, MD, PhD, Tatsusada Okuno, MD, PhD and Hideki Mochizuki, MD, PhD

Department of Neurology, Graduate School of Medicine, Osaka University, Suita, Osaka, Japan

Background: Glial fibrillary acidic protein (GFAP) and Neurofilament light chain (NfL) have been measured as biomarkers for neurological diseases. Simoa®, high sensitivity ELISA assay, is commonly used to measure these values, but there are some problems such as high cost, complicated protocols, etc. Recently Ella®, fully automatic ELISA assay was introduced and it is characterized by its great simplicity of operation. In this study, we used Ella for testing sample, with the aim of verifying homology with the data of Simoa. In addition, we aimed to verify whether GFAP and NfL concentrations show changes before and after treatment. Although several reports have already shown that GFAP is higher in NMOSD patients than normal people, there are no reports of changes in GFAP and NfL before and after treatment.
Methods: Values for identical samples (NMOSD and MS patients' serum) measured in the Ella and Simoa assays were compared. Next, GFAP and NfL concentrations are measured in serum of patients with AQP4-positive NMOSD in Ella. Serum samples were taken at attack (initial or recurrent) and after PE (plasma exchange), respectively. Values before and after PE were compared.
Results: NfL values were strongly correlated with Simoa and Ella. The GFAP test values were correlated with the Simoa values, which were approximately 26 times higher than the Ella values. About change of GFAP and NfL before and after PE, GFAP was high at the time of attack and decreased after PE. In contrast, the change of NfL is not consistent.
Conclusion: The Ella assay can be used as an alternative to the Simoa assay and it makes measurement of these proteins easier. Although there have been reports that GFAP values are associated with disease activity in NMOSD, changes before and after PE have not been reported, making this data very valuable.

Oral Session 2

Chair: Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)
Takayuki Kondo
(Kansai Medical University Medical Center)

OS2-2 Associations between the brain atrophy and clinical characteristics in patients with AQP4Ab+NMOSD

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Objectives: We aimed to compare the brain atrophy rate between patients with aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder without relapse during MRI intervals and age-sex-matched healthy controls (HCs) and to investigate the correlation between the clinical characteristics and brain atrophy rates in patients.

Methods: We grouped patients by age (≥55 years vs. <55 years) and performed age-sex-matching with Japanese Alzheimer's Disease Neuroimaging Initiative study or another study performed at our hospital, respectively. Statistical parametric mapping-12 with MATLAB was used to acquire NIfTI files, which were analyzed with the CIVET on the CBRAIN platform. We analyzed the harmonized values after eliminating the effect of MRI scanner difference by longitudinal ComBat. Clinical characteristics at baseline MRI included age, disease duration, Kurtzke's Expanded Disability Status Scale score, annualized attack rate, the number of attacks in the previous one or two years, the number of optic neuritis and myelitis, the maximum length of the spinal cord lesion, and the logarithm of the minimal angle of resolution (logMAR).

Results: We included 18 patients and 18 HCs. Patients showed the higher atrophy rate of normalized left temporal lobe compared with HCs. It positively correlated with the number of attacks in the previous two years, logMAR of the left eye, and the maximum spinal cord lesion length in patients.

Conclusions: The neuronal damages in the optic nerves or spinal cord may cause the higher left temporal lobe atrophy rate by axonal degeneration.

Oral Session 2

Chair: Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)
Takayuki Kondo
(Kansai Medical University Medical Center)

OS2-3 Investigation of Blood–Brain Barrier Dysfunction in Multiple Sclerosis According to Clinical Subtype and Genetic Background

Kinya Matsuo[1,2], Miwako Fujisawa[3], Yusei Miyazaki[4], Masaaki Niino[4], Juichi Fujimori[5], Ichiro Nakashima[5], Masayuki Nakamori[1], Britta Engelhardt[3], Hideaki Nishihara[1]

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Background: Multiple sclerosis (MS) is characterized by both inflammatory relapses and progressive neurodegeneration. While disease-modifying therapies are available, effective treatments for progressive MS remain limited. We previously established an *in vitro* model of the blood–brain barrier (BBB) using hiPSC-derived brain microvascular endothelial-like cells differentiated by the extended endothelial cell culture method (EECM-BMECs). Our data showed intrinsic BBB dysfunction as an independent determinant of MS disease subtype.

Methods: We expanded our hiPSC-derived EECM-BMECs modeling to include 19 MS patients representing various subtype (benign MS, RRMS, SPMS, PPMS) and 4 healthy controls. BBB integrity was assessed by evaluating (1) junctional localization of claudin-5 , (2) permeability to sodium fluorescein (NaFl), and (3) cell surface expression levels of adhesion molecules ICAM-1 and VCAM-1. Additionally, we compared RRMS-derived EECM-BMECs from Japanese and Swiss MS patients under an identical experimental protocol to investigate potential differences in BBB functions attributable to genetic background.

Results/Discussion: NaFl permeability was elevated in SPMS- and PPMS-derived BBB models, and showed variability among RRMS-derived EECM-BMECs. Disruption of junctional localization of claudin-5 correlated with increased BBB permeability across all MS subtypes. Upregulation of ICAM-1 and VCAM-1 was observed in hiPSC-BMECs derived from all MS patients. Notably, EECM-BMEC clones with higher permeability were more frequently observed in Swiss RRMS patients compared to Japanese RRMS-derived counterparts. These findings suggest that a greater proportion of patients with intrinsic BBB vulnerability may contribute to increased disease severity. This may also explain previously reported observations of milder disease phenotypes in Japanese MS patients compared to those from Western cohorts.

Conclusion: These results support that BBB dysfunction is a key feature contributing to progressive MS. Furthermore, inter-individual differences in genetic background may underlie variability in BBB integrity and may influence clinical disease course. Continued patient recruitment and molecular profiling will be essential to identify BBB-targeted therapeutic strategies, particularly for progressive forms of MS.

Oral Session 2

Chair: Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)
Takayuki Kondo
(Kansai Medical University Medical Center)

OS2-4 Efficacy and Fever-Associated Hospitalization Risk of Biologic Therapy in AQP4-IgG Positive NMOSD: A Retrospective Study

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Background: Biologic therapies have significantly improved relapse prevention in aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4-IgG+ NMOSD). However, the associated risks of fever and infection during treatment warrant careful evaluation.

Objective: To assess the efficacy and fever-related hospitalization risk of biologic therapies in patients with AQP4-IgG+ NMOSD.

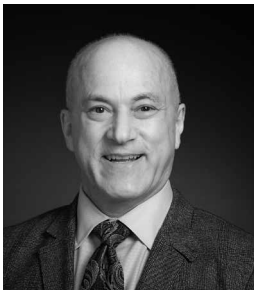
Methods: We conducted a retrospective chart review of 57 AQP4-IgG+ NMOSD patients treated at Keio University Hospital between 2015 and 2024. Annualized relapse rates (ARRs) were calculated for different treatment types: no treatment, steroid monotherapy, immunosuppressants, and biologics (C5 inhibitors, satralizumab, inebilizumab). Fever-associated hospitalizations—regardless of whether caused by infection or immune-mediated events—were analyzed in relation to treatment exposure.

Results: ARRs were 0.245 [0.158–0.380] for untreated periods, 0.155 [0.117–0.205] with steroid monotherapy, 0.206 [0.093–0.459] with immunosuppressants, and 0.038 [0.014–0.102] during biologic therapy. Across a cumulative observation period of 527.0 person-years, 21 hospitalizations for fever occurred (0.04/person-year). Of these, 17 occurred during biologic-exposed periods (92.9 person-years; 0.183/person-year), and 4 during non-biologic periods (434.0 person-years; 0.009/person-year). Blood cultures were obtained in 95% of hospitalizations and were all negative. A cause of fever was identified in 71% of cases, including COVID-19 (9 cases, 60%), urinary tract infection (1 case, 7%), aspiration pneumonia (1 case, 7%), drug-induced hypersensitivity syndrome (1 case, 7%), and central venous port infection (1 case, 7%). No invasive meningococcal infections were observed.

Conclusion: Biologic therapies are highly effective in preventing relapses in AQP4-IgG+ NMOSD. While fever-related hospitalizations were more frequent during biologic exposure, most cases were mild and non-invasive, often attributable to COVID-19 during the outbreak period. As the pandemic subsides, this risk is expected to decline, though continued vigilance remains important when initiating or maintaining biologic therapy.

Chair: Noriko Isobe
(Professor, Department of Neurology, Graduate School of Medical Sciences, Kyushu University)

SS-5 B cell Depletion Therapy for NMOSD: From Mechanisms to Management



Jeffrey L. Bennett, MD, PhD

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Neuromyelitis optica spectrum disorders (NMOSD) is a relapsing neuroinflammatory disorder of the CNS associated the production of pathogenic autoantibodies against the aquaporin-4 water channel (AQP4-IgG). In independent prospective clinical studies, B cell-depleting therapies (BCDT) targeting CD19 (inebilizumab) and CD20 (rituximab) have demonstrated the ability to diminish the frequency of NMOSD attacks relative to placebo. Inebilizumab has additionally demonstrated the ability to reduce the rates of MRI activity, disability progression, and hospitalization. Although serum titers of AQP4-IgG may lower following treatment with BCDTs, therapeutic benefit extends beyond the reduction of pathogenic autoantibody titers. Additional mechanisms of action include decreased memory B cell and extra-follicular plasmablast differentiation, increased regulatory B cell frequency and function, and depletion of proinflammatory immune cell populations. BCDTs show disparities in their depth, breadth, and effector mechanisms resulting in diverse treatment responses, side effect profiles, and pharmacogenetics. We will review the treatment of AQP4-IgG seropositive NMOSD with BCDTs focusing on utilizing our understanding of treatment benefits and risks to maximize disease management and minimize adverse events.

CURRICULUM VITAE

Dr. Jeffrey L. Bennett is the Gertrude Gilden Professor for Neurodegenerative Disease Research in the Departments of Neurology and Ophthalmology at the University of Colorado School of Medicine. He is also a faculty member of the Programs in Immunology and Neuroscience, and the Rocky Mountain MS Center at Anschutz Medical Campus.

Dr. Bennett received his medical and doctoral degrees at Stanford University and completed his internship and residency in Neurology at the University of Colorado and completed a clinical fellowship in neuro-ophthalmology at the University of Pennsylvania.

Dr. Bennett directs basic, translational, and clinical research programs on neuromyelitis optica spectrum disorder, multiple sclerosis, and MOGAD, and maintains active specialty practices in neuro-ophthalmology and neuro-immunology. Dr. Bennett has been a leader in understanding the role of B cells in demyelinating disorders. Using single cell recombinant monoclonal antibody technology, his laboratory has probed the targets of the immune response in NMOSD, MS, and MOGAD. His research in NMOSD has elucidated the pathogenicity of AQP4 autoantibodies and myelin targeted autoantibodies in MS. He is on the editorial board for the Annals of Neurology, Neurology: Neuroimmunology & Neuroinflammation; Multiple Sclerosis Journal, the Journal of Neuro-Ophthalmology, and Frontiers in Ophthalmology

P-1 Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease Presenting with Hydrocephalus Mimicking a Germ Cell Tumor: A Case Report

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Objective: Here, we report a case of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) that initially presented with hydrocephalus and mimicked a germ cell tumor.

Methods: A 23-year-old man presented with headache, nausea, and diplopia. Brain MRI revealed a lesion in the midbrain and thalamus, accompanied by obstructive hydrocephalus. Because of the suspicion of a germ cell tumor, neuroendoscopic third ventriculostomy and brain biopsy were performed on day 15 after symptom onset. Brain pathology revealed perivascular lymphocyte infiltration and demyelination, with no evidence of tumor. Postoperatively, headache and nausea improved; however, the patient's level of consciousness declined, and oculomotor nerve function worsened. Pulse steroid therapy was initiated as the lesion extended from the bilateral midbrain to the thalamus. Serum and cerebrospinal fluid tests for anti-MOG antibodies were positive, confirming the diagnosis of MOGAD. After plasmapheresis and a second course of steroid pulse therapy, the patient's neurological symptoms, including impaired consciousness, improved. Additional immunostaining revealed MOG loss and the proliferation of reactive astrocytes, mainly around blood vessels, consistent with MOGAD pathology. After one year, the patient experienced a relapse of the periaqueductal lesions and cortical encephalitis. Treatment with pulse steroid therapy and intravenous immunoglobulin resulted in a recovery without sequelae.

Results: MOGAD is an autoimmune demyelinating disorder of the central nervous system that can presents as optic neuritis, myelitis, or cortical encephalitis. Although tumor-like findings can be observed on brain MRI, hydrocephalus is a rare manifestation. Here, the differentiation from germ cell tumors, which typically arise in the pineal, hypothalamic, or pituitary regions of children and young adults, was challenging. A literature review revealed eight previously reported cases of inflammatory demyelinating diseases presenting with hydrocephalus, one of which was MOGAD.

Conclusions: MOGAD may initially present with tumor-like brain lesions, including hydrocephalus. In such cases, MOGAD must be considered as a differential diagnosis.

P-2 A case of tumefactive demyelination during B cell depletion therapy by ofatumumab

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Tumefactive demyelinating lesion (TDL) is a rare inflammatory disease of the central nervous system which can be accompanied by severe clinical presentations and require brain biopsy for a differential diagnosis. TDLs could be triggered by disease-modifying therapy for multiple sclerosis. However, it is unknown whether TDLs could emerge under B cell-depleted conditions by anti-CD20 treatment. We present a case of TDL that occurred during B-cell depletion therapy by ofatumumab and discuss its pathogenesis through serial magnetic resonance imaging and biopsied histopathology. The patient experienced longitudinal extensive transverse myelitis of unknown etiology at the age of 33. She had another myelitis five months later during oral prednisolone therapy, and ofatumumab was initiated thereafter. Eighteen months after ofatumumab initiation, she developed severe left hemiparesis and sensory loss. She has been negative for autoantibodies, including anti-aquaporin-4 and anti-myelin oligodendrocyte glycoprotein antibodies. Flow cytometry confirmed highly depleted B cells in peripheral blood. The serial MRI images revealed a trajectory of the lesion, characterized by perilesional edema, ring-enhancement, and hypointense signals on susceptibility-weighted images, suggesting prominent inflammation with intralesional microhemorrhage in the acute phase and subsequent perilesional iron deposition. The biopsied samples showed marked microhemorrhage, damaged vascular continuity, inflammatory cell infiltration except for CD20-expressing cells, mild perivenular loss of oligodendrocytes and astrocytes, and no perivascular deposition of activated complements. After repeated intravenous methylprednisolone and plasma exchanges, the TDL gradually shrank, although a perilesional hypointense ring remained on susceptibility-weighted images. TDLs can occur even during B-cell depletion therapy; however, the underlying mechanism is not fully elucidated.

P-3 Selection of disease-modifying drugs for pediatric multiple sclerosis with high disease activity.

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We report a case of a 7-year-old female patient with pediatric-onset multiple sclerosis (POMS), who initially presented with bilateral optic neuritis. During immunotherapy, a new lesion recurred in the internal capsule, indicating high disease activity. Oligoclonal bands (OBs) and anti-myelin oligodendrocyte glycoprotein (MOG) antibody were negative in cerebrospinal fluid. Anti-aquaporin-4 (AQP4) antibody was also negative in serum. We would like to discuss the selection of disease-modifying drugs (DMDs) for POMS in the context of this seronegative and clinically active case.

P-4 A Case of Immune-Related Triple M Syndrome with Subclinical Polyneuropathy

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A 74-year-old man underwent nephrectomy for left renal cell carcinoma and started pembrolizumab 70 days postoperatively (day 1). On day 21, he developed lower limb weakness and elevated creatine kinase (CK). Subsequently, he experienced diplopia, hoarseness, and dysphagia, leading to hospital admission on day 32. Elevated troponin I, ECG abnormalities, and cardiac MRI findings suggested myocarditis as an immune-related adverse events (irAE). Ptosis, diplopia, proximal muscle weakness, abnormal muscle MRI findings, and CK elevation were consistent with PD-1 myopathy and myasthenia gravis, for which corticosteroid therapy started. Muscle biopsy showed intense infiltration of lymphocytes and clustered necrotic/regenerating fibers, confirming a diagnosis of immune-related Triple M syndrome (myositis, myasthenia and myocarditis). Nerve conduction studies demonstrated demyelinating polyneuropathy. While ptosis and dysphagia improved, limb weakness still persisted, prompting the addition of intravenous immunoglobulin therapy. It is interesting that polyneuropathy was detected only through electrophysiological studies, without clear clinical correlation. This case highlights the importance of considering neurological symptoms consistent with polyneuropathy as subclinical peripheral neuropathy in association with irAE, and underscores the necessity of performing nerve conduction studies even in the absence of evident symptoms. In the context of irAE, subclinical peripheral neuropathy may coexist with the primary neurological manifestations. Accordingly, follow-up nerve conduction studies are essential for comprehensive evaluation. We will present the case with literature reviews.

P-5 Clinical evaluation of biologic agents used for treating neuromyelitis optica at our institution

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Background: Biologic agents play a crucial role in the treatment of neuromyelitis optica (NMO), a disease associated with a high risk of severe sequelae due to relapse. We conducted a clinical review of the biologic therapies used for treating patients with NMO at our hospital.

Methods: A retrospective analysis was performed using the medical records of patients with anti-aquaporin-4 antibody-positive NMO who were followed up as outpatients at our hospital as of April 2024. The use of biologic agents and the resulting outcomes were examined.

Results: Among 100 patients with NMO (mean age: 58.7 years), 70 had a history of biologic agent use. Biologic therapy was discontinued in four patients owing to the following reasons: transient disturbance of consciousness after ravulizumab administration (n=1), infections (n=2), and insufficient efficacy with satralizumab (n=1). The remaining 66 patients continued biologic treatment: 40, 22, and 4 with satralizumab, ravulizumab, and inebilizumab, respectively. The mean duration of biologic use was 12 years and 8 months in patients who transitioned from tocilizumab clinical trials, and 4 years and 4 months in others. The mean daily prednisolone dose was reduced from 9.9 mg at initiation to 2.9 mg by March 2025. Prednisolone was discontinued in 15 patients (22.7%), allowing monotherapy with biologics. The biologic agent was switched in 21 patients: from satralizumab to ravulizumab in 17 and to inebilizumab in 4. Among them, 12 experienced at least one relapse requiring hospitalization, and 9 showed gradual symptom progression without hospitalization. After switching, only two patients experienced relapse requiring hospitalization.

Conclusions: Biologic therapy is effective in reducing corticosteroid dosage in NMO. Additionally, switching to biologics in the event of relapse may improve relapse prevention.

P-6 Humanized-Aquaporin-4-Expressing Rat Created by Gene-Editing Technology and Its Use to Clarify the Pathology of Neuromyelitis Optica Spectrum Disorder

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Conventional rodent neuromyelitis optica spectrum disorder (NMOSD) models using patient-derived immunoglobulin G (IgG) are potentially affected by the differences between the human and rodent aquaporin-4 (AQP4) extracellular domains (ECDs). We hypothesized that the humanization of AQP4 ECDs would make the rodent model lesions closer to human NMOSD pathology. Humanized-AQP4-expressing (hAQP4) rats were generated using genome-editing technology, and the human AQP4-specific monoclonal antibody (mAb) or six patient-derived IgGs were introduced intraperitoneally into hAQP4 rats and wild-type Lewis (WT) rats after immunization with myelin basic protein and complete Freund's adjuvant. Human AQP4-specific mAb induced astrocyte loss lesions specifically in hAQP4 rats. The patient-derived IgGs also induced NMOSD-like tissue-destructive lesions with AQP4 loss, demyelination, axonal swelling, complement deposition, and marked neutrophil and macrophage/microglia infiltration in hAQP4 rats; however, the difference in AQP4 loss lesion size and infiltrating cells was not significant between hAQP4 and WT rats. The patient-derived IgGs bound to both human and rat AQP4 M23, suggesting their binding to the shared region of human and rat AQP4 ECDs. Anti-AQP4 titers positively correlated with AQP4 loss lesion size and neutrophil and macrophage/microglia infiltration. Considering that patient-derived IgGs vary in binding sites and affinities and some of them may not bind to rodent AQP4, our hAQP4 rat is expected to reproduce NMOSD-like pathology more accurately than WT rats.

P-7 Delayed Visual Improvement After Optic Neuritis in MOGAD: Case Report

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Optic neuritis associated with myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) can lead to residual visual impairment despite acute immunomodulatory treatment. We report a case that showed significant delayed visual improvement several months after acute therapy, despite initial persistent visual deficits.

A 38-year-old female developed MOGAD with brainstem encephalitis and myelitis at age 33. While on 3 mg/day of oral prednisolone (PSL), she experienced a relapse of left optic neuritis and brainstem encephalitis. Despite four courses of steroid pulse therapy and seven sessions of plasma exchange, her corrected visual acuity remained 0.2. After discharge, she started 10 mg/day PSL and 50 mg/day azathioprine. Her vision remarkably improved to 1.5 four months post-relapse.

This case highlights the importance of considering long-term visual improvement as a possibility in MOGAD-associated optic neuritis, even when initial acute treatment does not fully restore vision.

P-8 Selective Plasma Exchange Therapy for Acute-phase Treatment of Neuromyelitis Optica Spectrum Disorder: Cases series

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While plasma exchange (PE) is effective for the acute-phase treatment of neuromyelitis optica spectrum disorder (NMOSD), it often requires repeated transfusion of fresh frozen plasma (FFP) due to significant reductions in serum fibrinogen (Fbg). Selective plasma exchange (SePE), a modified form of PE, employs a plasma filtration membrane with pores approximately one-tenth the size of those used in conventional PE. SePE allows for the removal of immunoglobulin G (IgG) while preserving coagulation factors such as Fbg. However, its application in NMOSD has been rarely reported. We retrospectively examined AQP4-antibody-positive NMOSD patients admitted to our hospital between April 2018 and March 2025 who underwent SePE. Six patients (3 men) were included, with a median age at admission of 55 years (range: 17–83) and a median EDSS score of 7.0 (range: 3.0–8.0). All patients underwent PE after inadequate response to methylprednisolone pulse therapy (mPSL). Four patients were switched from PE to SePE, while two received SePE alone. The median number of SePE sessions was 4.5 (range: 4–7), and the median change in EDSS at the end of SePE was –2.0 (range: –4.5 to 0), with improvement observed in 5 of 6 patients (83%). All four patients who underwent PE required FFP transfusion, with a median volume of 2400 mL (range: 1520–3840 mL). In contrast, none of the patients required FFP transfusion following SePE. The mean IgG removal rate per session was 62% for PE and 61% for SePE; the mean Fbg removal rate was 73% for PE and 28% for SePE. SePE may offer a favorable therapeutic effect in the acute phase of NMOSD while avoiding FFP transfusion.

P-9 A brain-biopsied case of autoimmune GFAP astrocytopathy

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Glial fibrillary acidic protein (GFAP) is a major cytoskeletal protein of astrocytes. Autoantibodies against GFAP alpha in the cerebrospinal fluid (CSF) have been detected in some patients with meningoencephalomyelitis. Such inflammatory CNS disease with anti-GFAP alpha antibody has been proposed as "autoimmune GFAP astrocytopathy." We present a brain-biopsied case of the disease.

A 29-year-old man developed subacute nausea, vertigo, and gait instability. Brain MRI showed a tumefactive right cerebellar lesion, and FDG-and methionine-PET showed slightly increased uptake in the lesion. CSF cells and proteins were not increased, but oligoclonal IgG bands (OCB) were positive. Brain biopsy was done and the histopathological study demonstrated perivascular infiltration of CD68+macrophages and lymphocytes without cytological atypia. Immunostaining of GFAP, S-100, and beta-tubulin on astrocytes were preserved or relatively increased, reflecting reactive astrocytes. The diagnosis of inflammatory CNS disease was made, and high-dose corticosteroids were administered, resulting in clinical improvement and resolution of the lesion. After corticosteroids were tapered off, he developed subacute diplopia, left facial and upper limb weakness, and numbness in lower limbs 1.5 years later. Brain and spinal MRI revealed a T2 hyperintense lesion extending from medulla to upper cervical cord with swelling and punctate enhancement. AQP4 antibody and MOG antibody were negative and CSF study showed mild pleocytosis and OCB positivity. Corticosteroids were clinically effective as seen in the first attack. Afterward, he was found to be positive for anti-GFAP alpha antibody in the CSF. Throughout the clinical course, brain MRI showed no linear perivascular radial enhancement.

The present case is relapsing autoimmune GFAP astrocytopathy whose attacks showed good response to corticosteroid therapy. The pathological examination of the biopsied tumefactive cerebellar lesion demonstrated perivascular immune cell infiltration but no massive astrocyte loss like AQP4 antibody-positive neuromyelitis optica spectrum disorder.

P-10 Differential Serum ACE Levels in MOG-AD and Anti–AQP4 Antibody–Positive NMOSD

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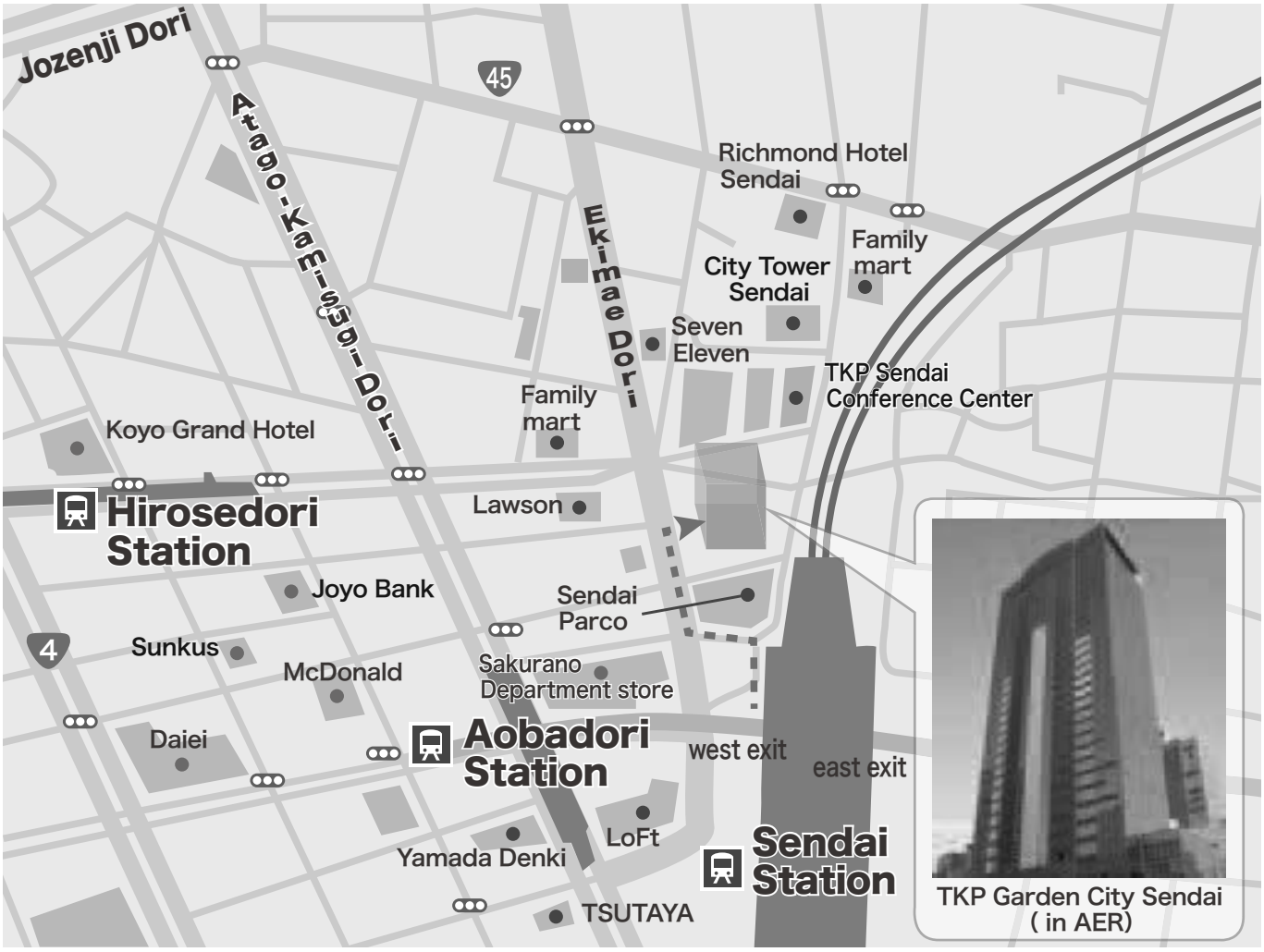
Background: Multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) are autoimmune diseases of the central nervous system with distinct pathophysiological mechanisms. Although their underlying biology has been increasingly elucidated, comparative studies on serum angiotensin-converting enzyme (ACE) levels across these disorders remain limited. This study aimed to investigate differences in serum ACE levels between myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOG-AD), and anti-aquaporin 4 (AQP4) antibody (AQP4-Ab) positive NMOSD, and to explore the potential clinical significance.

Methods: Serum ACE levels were measured prior to treatment in 25 patients with MOG-AD and 48 patients with NMOSD.

Results: The mean serum ACE levels were 8.90 U/L in the MOG-AD group and 10.64 U/L in the NMOSD group. Statistical analysis revealed a trend toward lower serum ACE levels in the MOG-AD group compared to the NMOSD group ($p = 0.0406$).

Conclusion: ACE is a component of the renin–angiotensin system (RAS), and its expression is known to be upregulated by inflammatory cytokines such as interleukin-6 and tumor necrosis factor-alpha. In MS and NMOSD, systemic immune activation involving T cells and B cells plays a central role in disease pathogenesis, which may account for relatively elevated serum ACE levels in these conditions. In contrast, the lower serum ACE levels observed in MOG-AD may reflect a more localized inflammatory process, as opposed to systemic immune activation. These findings suggest that serum ACE could serve as a biomarker reflecting the pattern and extent of inflammation and may be of potential utility in differentiating MOG-AD from NMOSD. Further studies are warranted to elucidate the mechanisms linking ACE regulation and the pathophysiology of MOG-AD.

Access



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