多発性硬化症および視神経脊髄炎に関する国際会議

Sendai Conference 2024

【 会　　期 】

2024年 7月 6日 (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

【 世 話 人 】

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中島　一郎
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【 共催企業 】

ALEXION AstraZeneca Rare Disease　Mitsubishi Tanabe Pharma　すべての革新は患者さんのために 中外製薬 ロシュ 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

Sendai Conference 2024運営事務局
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Sendai Conference 2024

Date: 6 July, 2024
Venue: Hall 21C, 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 Biogen Japan Ltd.)
11:00～11:15	Coffee Break
11:15～12:05	Sendai Conference Special Lecturers
12:05～13:00	Lunch & Poster Viewing / General Membership Meeting of NPO
13:00～13:10	Photo Session
13:10～14:00	Sponsored Session 2 (Sponsored by Mitsubishi Tanabe Pharma)
14:00～15:00	Oral Session 2
15:00～15:15	Coffee Break
15:15～16:05	Sponsored Session 3 (Sponsored by Alexion Pharma G.K.)
16:05～16:55	Sponsored Session 4 (Sponsored by Novartis Pharma K.K.)
16:55	Closing Remarks (& Award Ceremony)

Sendai Conference 2024 Program

9:00～ 9:05 Opening Remarks

OR Dr. Kazuo Fujihara

9:05～10:05 Oral Session 1 (Chair: Dr. Kazumasa Yokoyama & Dr. Tatsuro Misu)

OS1-1 Dr. Kimihiko Kaneko (Tohoku University)
Different CSF complement activation patterns following C5 cleavage in MOGAD and AQP4-IgG+NMOSD

OS1-2 Dr. Yuki Matsumoto (Tohoku University)
Dynamic Changes in Patient Admission and Their Disabilities in Multiple sclerosis and Neuromyelitis Optica: A Japanese Nationwide Administrative Data Study

OS1-3 Dr. Yoshiki Takai (Tohoku University)
Characteristic patterns of complement deposition in NMOSD, MOGAD and MS

OS1-4 Dr. Kazuo Fujihara (Fukushima Medical University / Southern TOHOKU Research Institute for Neuroscience)
Epidemiology of myelin oligodendrocyte glycoprotein antibody-associated disease in the world: an updated review

10:10～11:00 Sponsored Session 1 (Chair: Dr. Yusei Miyazaki)

SS-1 Dr. Monica Margoni (IRCCS San Raffaele Scientific Institute, Milan, Italy)
Improved understanding of multiple sclerosis through the lens of magnetic resonance imaging

(Sponsored by Biogen Japan Ltd.)

11:00～11:15 Coffee Break

11:15～12:05 Sendai Conference Special Lecturers (Chair: Dr. Izumi Kawachi)

SL-1 Dr. Ho Jin Kim (National Cancer Center, Korea)
Advances and Challenges in the Treatment of NMOSD in Korea

SL-2 Dr. Sung-Min Kim (Seoul National University Hospital)
Dr. Youn Nam Kwon (Severance Hospital / Yonsei University College of Medicine)
When to treat inflammatory demyelinating disease of the CNS: Report from Korean multicenter cohort

12:05～13:00 Lunch & Poster Viewing / General Membership Meeting of NPO

13:00～13:10 Photo Session

13:10～14:00 Sponsored Session 2 (Chair: Dr. Noriko Isobe)

SS-2 Dr. Orhan Aktas (Heinrich Heine University)
Title: TBD

(Sponsored by Mitsubishi Tanabe Pharma)

14:00～15:00 Oral Session 2 (Chair: Dr. Takayuki Kondo & Dr. Juichi Fujimori)

OS2-1 Dr. Hideaki Nishihara (Yamaguchi University)
Analyzing the Impact of Blood-Brain Barrier Dysfunction on Clinical Phenotypes in Multiple Sclerosis

OS2-2 Dr. Haruhiko Motegi (Keio University / Jikei University)
Non-Lesional White Matter Changes Depicted by *q*-Space Diffusional MRI Correlate with Brain Atrophy and Differ Between MS and NMOSD.

OS2-3 Dr. Akihito Hao (Tokyo Metropolitan Neurological Hospital)
Efficacy and safety of Glatiramer acetate

OS2-4 Dr. Tomoko Okamoto (National Center of Neurology and Psychiatry)
Phase Ⅱ Clinical Trial of NKT Cell-Targeting Glycolipid OCH-NCNP1 for Patients with Relapsing Multiple Sclerosis

15:00～15:15 Coffee Break

15:15～16:05 Sponsored Session 3 (Chair: Dr. Norio Chihara)

SS-3 Dr. Jeffrey Bennett (University of Colorado)
Complement C5 Inhibition: Reshaping the Treatment of Neuromyelitis Optica Spectrum Disorder

(Sponsored by Alexion Pharma G.K.)

16:05～16:55 Sponsored Session 4 (Chair: Dr. Koji Shinoda)

SS-4 Dr. Amit Bar-Or (University of Pennsylvania)
MS Pathogenesis, including microglia, and Immune Reconstitution after B-cell Therapy

(Sponsored by Novartis Pharma K.K.)

16:55 Closing Remarks (& Award Ceremony)

CR Dr. Ichiro Nakashima

Poster Session (Venue: Hall 21D)

P-1 Dr. Yoshiyuki Matsuki (Showa general Hospital / Tokyo Metropolitan Neurological Hospital)
Guillain-Barré syndrome preceded by posterior reversible encephalopathy syndrome

P-2 Dr. Fumitaka Shimizu (Yamaguchi University)
New microfluidic tri-culture BBB on-chips model for analysis of BBB disruption in NMOSD, MOGAD, and MS

P-3 Dr. Fumitaka Shimizu (Yamaguchi University)
A case of recurrent myelitis seronegative for anti-AQP4 antibody and anti-MOG antibody

P-4 Dr. Hanna Okada (Juntendo University)
Investigating Apathy in Autoimmune GFAP Astrocytopathy

P-5 Dr. Ritsu Akatani (Kobe University)
Exploring B Cell Dynamics through IL-6 Blockade in NMOSD

P-6 Dr. Hiroshi Kuroda (Fukushima Medical University / Southern TOHOKU Research Institute for Neuroscience)
A brain-biopsied case of autoimmune GFAP astrocytopathy

P-7 Dr. Haruhiko Motegi (Jikei University)
Combination Therapy with Ofatumumab and Erenumab in Multiple Sclerosis: A Case Report

Oral Session 1

Chair: Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)
Tatsuro Misu
(Department of Neurology, Tohoku University Graduate School of Medicine)

OS1-1 Different CSF complement activation patterns following C5 cleavage in MOGAD and AQP4-IgG+NMOSD

Kimihiko Kaneko[1], Hiroshi Kuroda[1,2,3], Yuki Matsumoto[1,4], Naohiro Sakamoto[1], Naoya Yamazaki[1], Naoki Yamamoto[1], Shu Umezawa[1], Chihiro Namatame[1], Hirohiko Ono[1], Yoshiki Takai[1], Toshiyuki Takahashi[1,5], Juichi Fujimori[6], Ichiro Nakashima[6], Yasuo Harigaya[7,8], Kazuo Fujihara[1,2,3], Tatsuro Misu[1], Masashi Aoki[1]

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3. Department of Multiple Sclerosis Therapeutics, Fukushima Medical University, Fukushima, Japan
4. Department of Neurology, NHO Miyagi National Hospital, Watari, Japan
5. Department of Neurology, NHO Yonezawa National Hospital, Yonezawa, Japan
6. Division of Neurology, Tohoku Medical and Pharmaceutical University, Sendai, Japan
7. Department of Neurology, Japanese Redcross Maebashi Hospital, Maebashi, Japan
8. Department of Neurology, Mihara Memorial Hospital, Isesaki, Japan

Objective: In myelin oligodendrocyte glycoprotein IgG-associated disease(MOGAD) and aquaporin-4 IgG+ neuromyelitis optica spectrum disorder (AQP4+NMOSD), the autoantibodies are mainly composed of IgG1, and complement-dependent cytotoxicity is a primary pathomechanism in AQP4+NMOSD. We aimed to evaluate the CSF complement activation in MOGAD.

Method: CSF-C3a, -C4a, -C5a, and -C5b-9 levels during acute phase before treatment in patients with MOGAD (n=12), AQP4+NMOSD (n=11), multiple sclerosis (MS) (n=5), and non-inflammatory neurologic disease (n=2) were measured.

Results: CSF-C3a and -C5a levels were significantly higher in MOGAD(mean±SD, 5629±1079 pg/ml and 2930±435.8 pg/ml) and AQP4+NMOSD(6017±3937 pg/ml and 2544±1231 pg/ml) than in MS (1507±1286 pg/ml and193.8±0.53 pg/ml). CSF-C3a, -C4a, and -C5a did not differ between MOGADand AQP4+NMOSD, whereas CSF-C5b-9 (membrane attack complex, MAC)levels were significantly lower in MOGAD (17.4±27.9 ng/ml) than in AQP4+NMOSD (62.5±45.1 ng/ml, p=0.0019). MOGAD patients with severer attacks [expanded disability status scale (EDSS)≥3.5] had higher C5b-9 levels(34.0±38.4 ng/m) than those with milder attacks (EDSS≤3.0, 0.9±0.7 ng/ml, p=0.044).

Discussion: The complement pathway is activated in both MOGAD and AQP4+NMOSD, but MAC formation is lower in MOGAD, particularly in those with mild attacks, than in AQP4+NMOSD. One possible explanation for the difference in C5b-9 level is CD59 expression. It is abundantly expressed on the surface of myelin, whereas weakly expressed on the astrocyte foot process, and works as inhibitory complement-regulatory protein to form MAC. Hence, MAC formation might be strictly and inhibitory regulated on the myelin. These findings may have pathogenetic and therapeutic implications in MOGAD.

Oral Session 1

Chair: Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)
Tatsuro Misu
(Department of Neurology, Tohoku University Graduate School of Medicine)

OS1-2 Dynamic Changes in Patient Admission and Their Disabilities in Multiple sclerosis and Neuromyelitis Optica: A Japanese Nationwide Administrative Data Study

Yuki Matsumoto[1], Kunio Tarasawa[2], Tatsuro Misu[3], Chihiro Namatame[1], Yoshiki Takai[1], Hiroshi Kuroda[1], Kazuo Fujihara[4], Kiyohide Fushimi[5], Kenji Fujimori[2], Masashi Aoki[3].

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4. Fukushima Medical University, Department of Multiple Sclerosis Therapeutics and Southern Tohoku Research Institute for Neuroscience, Multiple Sclerosis & Neuromyelitis Optica Center, Fukushima, Japan
5. Tokyo Medical and Dental University Graduate School of Medical and Dental Sciences, Department of Health Policy and Informatics, Tokyo, Japan

Background: The real-world data evidences how establishment of neuromyelitis optica (NMO) disease concept and development disease modifying therapy affect the patients with multiple sclerosis (MS) and NMO are lacking. The aim of this study is to clarify the diachronic trend of the severity and admissions of patients with MS and NMO.

Methods: We retrospectively investigated the trends in admissions, treatments, and disabilities in the patients with MS and NMO using the Japanese administrative data between 2012 and 2017.

Results: We analyzed acute stage 9,545 and 2,035 admissions in each 6,100 MS and 1,555 NMO patients. The annual number of admission in MS significantly decreased in 6 years; however, those in NMO consistently increased. The patient proportion with lower disability was significantly increased in MS and NMO. These trends were especially observed in patients admitted to centralized hospitals with more active treatments, such as second-line disease modifying therapy for MS and plasmapheresis for NMO. Patients with NMO using DMT for MS diminished in 6 years.

Conclusion: A gradual improvement of disability in patients with MS and NMO was observed, probably due to advanced treatments, increased NMO awareness, and decreased misdiagnosis, which seems to be the key for better prognosis in MS and NMO.

Oral Session 1

Chair: Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)
Tatsuro Misu
(Department of Neurology, Tohoku University Graduate School of Medicine)

OS1-3 Characteristic patterns of complement deposition in NMOSD, MOGAD and MS

Yoshiki Takai[1,2], Simon Hametner[3], Christian Riedl[3], Tatsuro Misu[1], Kazuo Fujihara[1,4], Romana Höftberger[3]

1. Department of Neurology, Tohoku University Graduate School of Medicine.
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4. Department of Multiple Sclerosis Therapeutics, Fukushima Medical University.

Background: The involvement of the complement system could be crucial in the pathogenesis of inflammatory demyelinating diseases (IDD). While complement inhibition significantly reduces a risk of relapse in NMOSD, no clear consensus has been reached on the role of complements in MOGAD and MS.
Objective: To compare complement deposition in NMOSD, MOGAD and MS.
Methods: We examined CNS tissues from patients with NMOSD (14 autopsies), MOGAD (5 autopsies and 14 biopsies) and MS (17 autopsies). Using immunohistochemistry, we evaluated the deposition of three complement pathway products (C3d, C4d, and C9neo) in relation to demyelination and astrocyte damage.
Results: The median (range) of age (years) at the time of tissue acquisition was NMOSD: 52(20-78), MOGAD: 34.5(4-67) and MS: 51(28-76), and the sex ratio (F/M) was NMOSD: 12/2, MOGAD: 11/9, and MS: 12/7. In NMOSD and MOGAD, the perivascular complement deposition was predominant, with a typical rim/rosette pattern for all three complement products in the acute phase of NMOSD. In total, C4d deposition was seen in 96% of active demyelinating lesions in MOGAD, while C3d and C9neo deposition were present in fewer (74% and 64%, respectively). Interestingly, C9neo was also deposited in 78% (range: 67-95%) of perivascular C4d deposits in acute lesions among NMOSD cases, while such double-deposited lesions were only seen 25% (range: 0-100%) in MOGAD. Thus, C9neo deposition was relatively milder compared to C4d and C3d deposition, although there were remarkable inter-individual differences in MOGAD. In MS, C3d and C9neo deposits were relatively small in amount, while C4d deposits were clearly present, surrounding the rims of demyelinating lesions. This finding is characteristic of MS, especially in cases with slowly expanding lesions.
Conclusion: We found characteristic patterns of complement deposition in the three IDD, potentially related to differences in pathogenesis of those diseases.

Oral Session 1

Chair: Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)
Tatsuro Misu
(Department of Neurology, Tohoku University Graduate School of Medicine)

OS1-4 Epidemiology of myelin oligodendrocyte glycoprotein antibody-associated disease in the world: an updated review

Kazuo Fujihara[2,3], Jyh Yung Hor[1], Hiroshi Kuroda[2,3],

1. Department of Neurology, Penang General Hospital, Penang, Malaysia.
2. Department of Multiple Sclerosis Therapeutics, Fukushima Medical University School of Medicine, Koriyama, Japan.
3. Multiple Sclerosis and Neuromyelitis Optica Center, Southern TOHOKU Research Institute for Neuroscience, Koriyama, Japan.

Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOGAD) is an inflammatory demyelinating disease of the central nervous system (CNS) with conformation-sensitive MOG antibodies. The spectrum of MOGAD includes monophasic/relapsing optic neuritis, myelitis, neuromyelitis optica spectrum disorder (NMOSD) phenotype without aquaporin 4 (AQP4) antibodies, acute/multiphasic demyelinating encephalomyelitis (ADEM/MDEM)-like presentation, and brainstem and cerebral cortical encephalitis. Unlike AQP4+ NMOSD, there is no apparent female preponderance in MOGAD, and MOGAD can onset in all age groups (average onset age is approximately 30 years). While prevalence and incidence data have been available for AQP4+ NMOSD globally, such data are only beginning to accumulate for MOGAD. We reviewed the currently available data from population-based MOGAD studies conducted around the world: three studies in Europe, three in Asia, and one joint study in the Americas. The prevalence of MOGAD is approximately 1.3-2.5/100,000, and the annual incidence is approximately 3.4-4.8 per million. Among White people, the prevalence of MOGAD appears to be slightly higher than that of AQP4+ NMOSD. No obvious latitude gradient was observed in the Japanese nationwide survey. The data available so far showed no obvious racial preponderance or strong HLA associations in MOGAD. However, precedent infection was reported in approximately 20-40% of MOGAD cases, and this is worthy of further investigation. Co-existing autoimmune disorders are less common in MOGAD than in AQP4+ NMOSD, but NMDAR antibodies may occasionally be positive in patients with MOGAD.
We will present updated epidemiological data in the world.

Sponsored Session 1

Chair: Yusei Miyazaki
(Department of Neurology, National Hospital Organization Hokkaido Medical Center)

SS-1 Improved understanding of multiple sclerosis through the lens of magnetic resonance imaging

Monica Margoni

Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy

Magnetic resonance imaging (MRI) plays a pivotal role in the diagnosis of multiple sclerosis (MS), in the monitoring of disease course and treatment response.

New evidence from the application of MRI in patients with clinically isolated syndromes has guided the 2017 revision of the McDonald criteria for MS diagnosis, which has simplified their clinical use while preserving accuracy. Other MRI measures may improve diagnostic specificity, but their assessment still needs to be standardized, and their reliability confirmed. Novel MRI techniques are providing fundamental insights into the pathological substrates of the disease and are helping to give a better understanding of its clinical manifestations. Combined clinical-MRI measures of disease activity and progression, together with the use of clinically relevant MRI measures might improve treatment monitoring.

In this view, the application of artificial intelligence, through the integration of clinical and MRI data, may allow for disease classification, prediction of disease progression and treatment responses.

CURRICULUM VITAE

Dr. Monica Margoni is currently Neurologist and Senior Researcher at the Neuroimaging Research Unit, Division of Neuroscience, Neurology and Neurorehabilitation Units, IRCCS San Raffaele Scientific Institute, Milan, Italy.

She received her medical degree in 2012 at the University of Padua, Italy. She performed her residency in Neurology (from 2013 to 2018) and her PhD in Neuroscience (from 2018 to 2021) at the University of Padua, Italy. During these periods, she has been also visiting research fellow at Mount Sinai Hospital in New York, United States (2018), under the supervision of Professor Matilde Inglese and Professor Fred Lublin, and MAGNIMS/ECTRIMS research fellow (from 2020 to 2022) at San Raffaele Hospital and Vita-Salute San Raffaele University, Milan, Italy, under the supervision of Professor Massimo Filippi and Professor Maria Rocca.

Her research activity is mainly focused on the application of Magnetic Resonance Imaging (MRI) in multiple sclerosis, especially in pediatric patients, and other demyelinating diseases to improve diagnostic criteria, to better define its pathophysiological substrates, the mechanisms leading to progressive accumulation of irreversible physical disability and cognitive impairment in such disorders and to monitor treatment response.

Sendai Conference Special Lecturers

Chair: Izumi Kawachi
(Niigata University)

SL-1 Advances and Challenges in the Treatment of NMOSD in Korea

Ho Jin Kim, MD, PhD

Department of Neurology, National Cancer Center, Goyang, Republic of Korea

Neuromyelitis Optica Spectrum Disorder (NMOSD) is a devastating autoimmune disorder of the central nervous system, characterized by unpredictable attacks that can cause severe, irreparable disability, even from a single episode. Recent advancements in understanding NMOSD pathophysiology have led to the development of targeted therapies, significantly enhancing the treatment landscape in Korea.

Acute management of NMOSD attacks in Korea primarily involves high-dose intravenous corticosteroids and plasmapheresis (and/or IVIG) for severe or refractory cases. This approach has proven effective, underscoring the necessity of rapid intervention to prevent long-term disability. For long-term management, the introduction of targeted therapies such as eculizumab, satralizumab, and inebilizumab has shown promising results in reducing relapse rates and improving patient quality of life. Traditional immunosuppressive treatments, including azathioprine, mycophenolate mofetil, and rituximab, also remain widely used.

Despite these advancements, challenges, particularly in treatment accessibility, persist. Continued efforts are needed to address these issues and ensure equitable access to these treatments, ultimately improving patient outcomes and quality of life.

In this talk, I will review the current state of NMOSD treatment in Korea, highlighting recent advancements and ongoing challenges

CURRICULUM VITAE

Dr. Ho Jin Kim serves as the Head of the Department of Neurology at the National Cancer Center, Korea, concurrently holding a professorship at the National Cancer Center Graduate School of Cancer Science & Policy.

He obtained his medical degree, as well as a master's degree and doctorate, from Seoul National University, where he also completed his residency in neurology, along with clinical fellowships in multiple sclerosis and neuromuscular disease. Dr. Kim furthered his academic pursuits as a research fellow in neuroimmunology at the University of Southern California, USA. Then he spent four years as a senior fellow and staff researcher in MS and neuroimmunology at the Montreal Neurological Institute of McGill University, Canada.

His primary research focus centers on autoimmune inflammatory diseases of the CNS, encompassing multiple sclerosis, neuromyelitis optica spectrum disorder, and MOG-IgG associated disease.

Dr. Kim has authored over 240 peer-reviewed articles in esteemed academic journals. Presently, he holds the position of vice-president at PACTRIMS and of president at the Korean Society of Neuroimmunology. Additionally, he serves as a co-editor for the Multiple Sclerosis Journal and an associate editor for the Journal of Clinical Neurology.

Chair: Izumi Kawachi
(Niigata University)

SL-2 When to treat inflammatory demyelinating disease of the CNS: Report from Korean multicenter cohort

Young Nam Kwon, M.D.Ph.D.[1], Sung Min Kim M.D.,Ph.D.[2]

1. Department of Neurology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea,
2. Department of neurology, Seoul National University Hospital

Multiple Sclerosis (MS), Neuromyelitis optica spectrum disorder (NMOSD), and MOG antibody-associated disease (MOGAD) are the two most common inflammatory demyelinating disease of the central nervous system (IDD). Recent development in academic and pharmaceutical field enabled diverse treatment options, which contributed significantly to improving the prognosis of patients with IDD. In addition to “which drug should be prescribed” issues, “when to treat patients with this drug” can be also important issue for better prognosis of patients. Here, we will discuss on these therapeutic time window with recent several multicenter study results from Korea,

CURRICULUM VITAE

[General Information]

Name:Sung Min Kim

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[Research Interests]

Multiple sclerosis, neuromyelitis optica, MOG-Ab associated disorder, Neuroimmunology

Oral Session 2

Chair: Takayuki Kondo
(Kansai Medical University Medical Center)
Juichi Fujimori
(Tohoku Medical and Pharmaceutical University)

OS2-1 Analyzing the Impact of Blood-Brain Barrier Dysfunction on Clinical Phenotypes in Multiple Sclerosis

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

1. Yamaguchi University,
2. Yamaguchi Prefectural Grand Medical Center
3. Theodor Kocher Institute, University of Bern
4. National Hospital Organization Hokkaido Medical Center
5. Tohoku Medical and Pharmaceutical University

Objective/Background: The breakdown of the blood-brain barrier (BBB), a major pathological feature of multiple sclerosis (MS), is generally considered a secondary result of central nervous system inflammation. However, we have recently demonstrated direct involvement of BBB breakdown in MS pathogenesis by establishing a BBB model from MS patients. This study aims to verify the possibility that the genetic vulnerability of the BBB influences the clinical phenotype of MS.

Methods: We enrolled MS patients with different clinical phenotypes (2 cases of benign MS, 5 cases of RRMS, and 2 cases of SPMS) as well as 5 healthy individuals. Using a differentiation method developed from iPSCs, we induced BBB-forming endothelial cells (BMEC-like cells) and verified BBB properties by analyzing the expression and localization of claudin-5, small molecule permeability, and the expression and functions of ICAM-1 and VCAM-1.

Results: Claudin-5 exhibited continuous expression in BMEC-like cells derived from healthy controls, with interruptions observed in RRMS patients and more severe disruptions noted in SPMS cases. Small molecule permeability was comparable between the benign MS group and healthy individuals, varied among RRMS cases, and was elevated in SPMS cases. The expression of adhesion molecules for immune cell infiltration was consistently elevated in all MS phenotypes compared to healthy individuals, with a more pronounced trend observed in SPMS.

Conclusion: Genetic vulnerability of the BBB was more pronounced in progressive MS. Predicting clinical phenotypes is crucial for individualized medicine in today's diverse clinical landscape. We plan to increase the number of cases and develop biomarkers for predicting clinical phenotypes targeting the BBB in the future.

Oral Session 2

Chair: Takayuki Kondo
(Kansai Medical University Medical Center)
Juichi Fujimori
(Tohoku Medical and Pharmaceutical University)

OS2-2 Non-Lesional White Matter Changes Depicted by *q*-Space Diffusional MRI Correlate with Brain Atrophy and Differ Between MS and NMOSD.

Haruhiko Motegi[1,2], Kenji Kufukihara[1,3], Satoshi Kitagawa[1,4], Koji Sekiguchi[1], Junichi Hata[5–7], Hirokazu Fujiwara[8] Masahiro Jinzaki[9], Hideyuki Okano[6,7], Masaya Nakamura[10], Yasuyuki Iguchi[2], Jin Nakahara[1]

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4 Department of Neurology, Inagi Municipal Hospital
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7. Laboratory for Marmoset Neural Architecture, RIKEN Center for Brain Science, Wako, Japan
8. Center of Preventive Medicine, Keio University School of Medicine, Tokyo, Japan
9. Department of Radiology, Keio University School of Medicine, Tokyo, Japan
10. Department of Orthopedic Surgery, Keio University School of Medicine, Tokyo, Japan

Background: We previously developed an optimized *q*-space diffusional MRI technique (normalized leptokurtic diffusion [NLD] map) to delineate the demyelinated lesions of multiple sclerosis (MS) patients (Fujiyoshi et al., J Neurosci 2016). We also revealed the associations between white matter (WM) changes and physical and cognitive disabilities in MS by using NLD index (Motegi et al., J Neurol Sci 2024). We aimed to determine the utility of *q*-space diffusional MRI in discerning the correlation of WM abnormality with brain atrophy in MS and detecting the difference in WM changes by utilizing the NLD index between MS and neuromyelitis optica spectrum disorder (NMOSD).

Methods: We conducted a retrospective observational study of MS and NMOSD patients treated at our hospital (Jan. 2012 to Oct. 2024). Clinical and MRI data were collected; Processing Speed Test (PST) data were obtained when possible. For a quantitative analysis of the NLD maps, we calculated the NLD index as previously reported. The third ventricle width was calculated as an indicator of brain atrophy.

Results: 101 MS patients and 15 NMOSD patients were examined. The lower corpus callosum and non-lesional WM NLD index were associated with worse Expanded Disability Status Scale (EDSS) and PST scores. The NLD indexes in the corpus callosum ($r= -0.64$, $p<0.0001$) and non-lesional white matter ($r= -0.45$, $p<0.0001$) were negatively associated with the width of the third ventricle in MS. When EDSS stratified severity, there was no difference in NLD indexes between MS and NMOSD for EDSS below 3. However, for EDSS 3 and above, The NLD indexes in the corpus callosum ($p=0.0136$) and non-lesional white matter ($p=0.0293$) were significantly lower in MS.

Conclusion: The NLD index is associated with brain atrophy in MS. It may reflect myelin abnormalities and detect differences in non-lesional white matter pathology during the progressive stages of MS and NMOSD.

Oral Session 2

Chair: Takayuki Kondo
(Kansai Medical University Medical Center)
Juichi Fujimori
(Tohoku Medical and Pharmaceutical University)

OS2-3 Efficacy and safety of Glatiramer acetate

Akihito Hao[1], Yoko Warabi, Kazushi Takahashi

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Background and objective: Glatiramer acetate (GA) has been used as a disease-modifying drug (DMD) for relapsing-remitting multiple sclerosis (RRMS) since its launch in Japan (2015). In this study, we aimed to evaluate its efficacy and safety in a real clinical setting.
Methods: We conducted a single-center retrospective study of the patients with RRMS who were admitted to our department between November 2015 and April 2024 and have been treated with GA.
Results: Twenty-two patients with RRMS (16 females and 6 males) were included in this study. The mean ages at disease onset and introduction of GA were 33.8±2.3 and 38.0±2.7 years, respectively. In addition, the mean follow-up period and duration of GA administration were 6.0±0.7 and 2.8±0.5 years, respectively. Under the administration of GA, the mean annualized relapse rate was 1.1±0.5. During the follow-up period, 10 patients (45.5%) could continue the treatment for its effectiveness, but 12 patients (54.5%) switched to different DMD (Dimethyl fumarate: 6 patients, Fingolimod 4 patients, Ofatumumab: 2 patients, and Siponimod: 1 patient). The reasons for the switch were as follows: ineffectiveness in 9 patients, a side effect in 1 patient, transition from RRMS to secondary progressive MS (SPMS) in 1 patient, and dislike of subcutaneous infection in 1 patient. As to adverse events, only 1 patient had to discontinue GA for liver dysfunction, and the others were injection site reactions or temporary side effects. In addition, 2 female patients delivered their babies safely (1 patient discontinued and the other continued GA during pregnancy).
Conclusions: GA was well tolerated with few severe side effects and safe in pregnancy. In addition, it was effective for relapse prevention in approximately half of the RRMS patients, but escalation of DMD was needed in the other half.

Oral Session 2

Chair: Takayuki Kondo
(Kansai Medical University Medical Center)
Juichi Fujimori
(Tohoku Medical and Pharmaceutical University)

OS2-4 Phase II Clinical Trial of NKT Cell-Targeting Glycolipid OCH-NCNP1 for Patients with Relapsing Multiple Sclerosis

Tomoko Okamoto[1], Wakiro Sato[2], Youwei Lin[1], Yukio Kimura[3], Noriko Sato[3], Takami Ishizuka[4], Harumasa Nakamura[4], Sachiko Miyake[5], Yuji Takahashi[1], Takashi Yamamura[6]

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Objective: To investigate the efficacy and safety of the glycolipid OCH-NCNP1 (OCH), in patients with relapsing multiple sclerosis (RMS).

Background: First-in-human clinical trial of OCH, orally administered to healthy subjects and multiple sclerosis (MS) patients has demonstrated immunoregulatory effects through activation of NKT cells.

Methods: A randomised, placebo-controlled study was conducted with a placebo group (n=15) and an OCH group (n=15) in 30 RMS patients. OCH (3.0 mg) or the placebo were orally administered weekly for 24 weeks. The primary outcomes were changes in magnetic resonance imaging results. Secondary outcomes were clinical observations, safety profiles, and exploratory biomarkers.

Results: Of the 30 enrolled patients [relapsing-remitting MS (RRMS): 18 patients and secondary progressive MS (SPMS): 12 patients], 25 completed the trial, while 5 discontinued. In comparison with the placebo group, patients in the OCH group tended to have fewer new lesions or existing enlarged lesions, a lower annual recurrence rate, and more cases achieving NEDA, although there were no significant differences. Regarding the cumulative recurrence-free rate, MS activity was more suppressed in the OCH group than in the placebo group. The MS subtype analysis revealed that patients with SPMS in the OCH group significantly achieved NEDA (5/6 patients; 83.3%) compared with those in the placebo group (0/6 patients; 0%; p=0.015). Biomarker analysis revealed a significant increase in IL-4-producing helper T cells on day 1 after OCH administration compared with the placebo (p=0.010). The frequency of granulocyte-macrophage colony-stimulating factor (GM-CSF)-producing helper T-cells at 6 months after OCH administration significantly decreased compared with pre-treatment values (p=0.0056). A more significant decrease was observed in the SPMS group than in the RRMS group. There was no significant difference between the OCH and placebo groups in the safety profile.

Conclusions: OCH is a promising treatment for multiple sclerosis, especially for SPMS.

Chair: Norio Chihara
(Division of Neurology, Kobe University)

SS-3 Complement C5 Inhibition: Reshaping the Treatment of Neuromyelitis Optica Spectrum

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Neuromyelitis optic spectrum disorder (NMOSD) is a rare autoimmune inflammatory disorder of the central nervous system (CNS) targeted against the aquaporin-4 (AQP4) water channel (AQP4). 90% of NMOSD patients are seropositive for pathogenic AQP4 autoantibodies (AQP4-IgG) that initiate complement-dependent cytotoxicity (CDC) on target astrocytes. AQP4-IgG activation of the classical complement pathway results in membrane attack complex formation, polymorphonuclear cell recruitment, activation, and degranulation.

Animal models of NMOSD demonstrate that CDC is essential for astrocyte destruction, and Phase 3 clinical trials for the C5 complement inhibitor therapies (C5ITs) eculizumab and ravalizumab have demonstrated >94% reduction in the risk of relapse in AQP4-IgG seropositive NMOSD patients. Following mandatory meningococcal vaccination, treatment with eculizumab or ravalizumab was associated with manageable treatment-related adverse events. Glial fibrillary acidic protein (GFAP) and neurofilament light chain (NfL) levels, biomarkers of astrocyte and neuronal injury, were quickly diminished by C5IT and levels continued to decrease during treatment.

Understanding the mechanisms driving complement activation and downstream CNS tissue injury is essential for limiting disability in NMOSD patients. We will examine how AQP4-IgG is engineered for efficient complement activation on CNS astrocytes, and how C5IT may hold promise beyond NMOSD relapse prevention to rapidly arrest acute CNS injury and facilitate repair.

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, optic neuritis, and MOGAD, and maintains active specialty practices in neuro-ophthalmology and neuro-immunology. He has received the Stephen Reingold Award from the National Multiple Sclerosis Society and the CU Inventor of the Year Award from the University of Colorado.

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.

Sponsored Session 4

Chair: Koji Shinoda
(Chief physician, Department of Neurology, Iizuka Hospital, Japan Research Assistant Professor, Department of Neurology, Graduate School of Medical Sciences, Kyushu University)

SS-4 MS Pathogenesis, including microglia, and Immune Reconstitution after B-cell Therapy

Amit Bar-Or, MD FRCPC

Melissa and Paul Anderson Distinguished Chair
Director, Center for Neuroinflammation and Experimental Therapeutics and Chief, Multiple Sclerosis Division, Department of Neurology Perelman Center for Advanced Medicine (PCAM), University of Pennsylvania

Though multiple sclerosis (MS) has traditionally been viewed as a T-cell mediated disease, recent years have underscored roles of B cells in MS disease pathogenesis. Among these, antibody-independent functions of B cells are thought to contribute to both relapsing and progressive disease processes. We will overview mechanisms by which B cells and their functionally distinct subsets bidirectionally interact with T cells and myeloid cells in the periphery where they mediate relapsing MS disease biology, as well as how such subsets are thought to interact with both infiltrating immune cells and CNS resident glial cells (including microglia) thereby contributing to smoldering CNS-compartmentalized inflammation and progressive disease biology. A novel mechanism involving immune-metabolism will be described that regulates the balance between pro-and anti-inflammatory B cell cytokine responses, thereby modulating myeloid cell responses. Finally, the therapeutic mode of action of current and future B-cell targeting therapies will be considered as well as the biological rationale for why transient B-cell depletion and subsequent reconstitution may be associated with durable remission.

CURRICULUM VITAE

Dr. Bar-Or holds the Melissa and Paul Anderson President's Distinguished Chair at the University of Pennsylvania, where he Directs the Centre for Neuroinflammation and Experimental Therapeutics (CNET) and serves as Chief of the Division of Multiple Sclerosis (MS) and related disorders. His clinical focus is on MS and other neuroinflammatory disorders, in both adults and children.

Following an undergraduate degree at McMaster University, Dr. Bar-Or earned his medical degree at McGill University, Montreal, Québec, also completing the Clinical Investigator Training Program (CITP) leading to a master's degree in Medical Science and Translational Research at HMS and the Massachusetts Institute of Technology (MIT), with additional training through the Harvard School of Public Health Certificate Program in Clinical Effectiveness. He then joined the Department of Neurology and Neurosurgery at the Montreal Neurological Institute and Hospital, McGill University, where he attained tenured Professor rank in 2012 and subsequently also served as the Institute's Associate Director for Translational Research prior to arriving at Penn.

Dr. Bar-Or's research focuses on neuroimmune health and central nervous system (CNS) inflammatory diseases across the age span. Major contributions have included discovery of cellular mechanisms by which human T cell, B cell, and myeloid cell subsets modulate one another and interact with brain cells; elucidating the mode-of-action of experimental therapies; advancing the development of clinically meaningful biomarkers; and developing precision medicine strategies for autoimmune and CNS inflammatory diseases. For his work. Dr. Bar-Or has received multiple awards including the 2021 prestigious Barancik Prize for Research Innovation in MS.

P-1 Guillain-Barré syndrome preceded by posterior reversible encephalopathy syndrome

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Guillain-Barré Syndrome (GBS) is generally known to develop symptoms after infection and posterior reversible encephalopathy syndrome (PRES) rarely precedes GBS. We report a 56-year-old male patient who developed GBS preceded by PRES.

The patient experienced headache, blurred vision, hypertension and a seizure three days after mountain climbing. The next day, he was admitted to a psychiatric hospital due to anxiety, agitation and urinary retention. Over the next five days, facial paralysis, limb weakness and sensory disturbance appeared and he was transferred to our hospital. Brain MRI showed fluid-attenuated inversion recovery (FLAIR) hyperintensity lesions in the bilateral occipital regions, but the lesions disappeared 8 days after admission. Lumbar spine MRI showed a remarkable contrast effect of the lumber nerve root and cauda equina. Nerve conduction studies showed prolonged distal latency, conduction block, and decrease in the amplitude of compound muscle action potentials and in motor nerve conduction velocity. Serum anti-GM1 antibody was positive. Cerebrospinal fluid analysis showed elevated protein. Despite initial suspicion of Lyme disease because his disease occurred after mountain climbing, antibody test was negative. We diagnosed his disease as GBS preceded by PRES. Hypertension recovered without any treatment. After plasma exchange and intravenous methylprednisolone therapy, his symptoms came to recover and he was transferred to another hospital for further rehabilitation. Five months later, he was able to walk without a cane.

GBS is rarely associated with PRES and what is more, GBS preceding PRES is even rare. Since the seizure and blurred vision were caused by occipital lobe lesions and the occipital lobe lesions were reversible, we consider that this patient had PRES. The absence of other factors causing PRES suggested that autonomic symptoms of GBS was the cause of PRES. When PRES is associated with autonomic symptoms, GBS should be considered in the differential diagnosis.

P-2 New microfluidic tri-culture BBB on-chips model for analysis of BBB disruption in NMOSD, MOGAD, and MS

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Background: Breakdown of the blood-brain barrier (BBB) is an important step for the pathomechanism of neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), and multiple sclerosis (MS).

Objective: To establish new microfluidic human tri-culture BBB on chips model in order to evaluate barrier dysfunction using our immortalized human brain endothelial cells (TY10), pericytes, and astrocytes.

Methods: TY10 were cultured under flow using Organoplate 3-lane (Mimetas) and formed a microvascular structure. Pericytes and astrocytes were co-cultured in the basal side surrounding TY10 microvascular, looking like 3D microvessels. Barrier function was evaluated by 20kDa-dextran leakage assay.

Results: Immunostaining of both nuclear and actin staining showed that TY10 cells form a vessel-like tubule structure in the top lane of Organoplate 3-lane after 10-day culture. Pericytes and astrocytes were seeded in the middle ECM lane and TY10 tri-cultured with pericytes and astrocytes constructed a tube-like structure. Leakage of 20-kDa dextran in co-cultured model with pericytes were lower than that in mono cultured model. Tri-cultured model also showed barrier function.

Conclusion: We developed a novel human BBB on a chip for the modelling of barrier dysfunction. We plan to use this model in order to elucidate the pathomechanism of BBB dysfunction in NMOSD, MOGAD and MS.

P-3 A case of recurrent myelitis seronegative for anti-AQP4 antibody and anti-MOG antibody

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We report a case of recurrent myelitis, who are seronegative for anti-AQP4 antibodies and anti-MOG antibodies, but are seropositive for anti-GRP78 antibody. 43-year-old male were admitted to our hospital due to muscle weakness and sensory disturbance of lower limbs. MRI showed the longitudinally extensive transverse myelitis (LETM) on Th5-10 and 2 brain lesions with open-ring enhancement. We suspected neuromyelitis optica spectrum disorder (NMOSD) and treated with intravenous methylprednisolone pulse therapy (1000mg for 3 days at 3 times) and plasmapheresis (total 7 times). His symptoms were completely recovered 2 months after initiation of treatment. He took prednisone (15mg/day) for relapse prevention. He relapsed bilateral lower limb paralysis and sensory impairment 2 months after onset. MRI showed the Gd-enhancement on spinal (Th5, Th7-9) and 3 brain lesions. After intravenous methylprednisolone pulse therapy (1000mg for 3 days at 3 times), symptoms are improved. He relapsed 3 months after onset. Autoantibodies associated with collagen disease was negative, but anti-Thyroid Peroxidase (TPO) antibody was positive. AQP4 autoantibodies were negative by both ELISA and cell-based assay (CBA) and MOG antibodies in both sera and CSF were negative by CBA. CSF analysis showed that normal cell count, increased protein (44.4mg/dl), absence of oligoclonal band and increased myelin basic protein (500pg/ml). Serum anti-GRP78 antibody was positive. We suspected seronegative NMOSD or atypical MS and treated with ofatumumab therapy. No recurrence was observed a month after treatment of ofatumumab.

P-4 Investigating Apathy in Autoimmune GFAP Astrocytopathy

Hanna Okada, Yasunobu Hoshino, Davide Cossu, Yuji Tomizawa, Kazumasa Yokoyama, Nobutaka Hattori

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Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy is an immune-mediated central nervous system disorder that has recently been established as a new disease concept. While the symptoms are often nonspecific, such as meningoencephalitis, there has been little mention of apathy so far. In this study, we examined apathy in GFAP astrocytopathy based on cases experienced at our hospital. The average age of onset was 42.2 ± 18.7 years, and males were more common at 3/5. Apathy was observed in 4/5 cases, with one case presenting apathy as the sole symptom at the time of consultation. Other symptoms included headache/fever in 2/5, impaired consciousness in 3/5, cognitive impairment in 2/5, motor impairment in 4/5, and autonomic dysfunction in 1/5. All cases showed increased cerebrospinal fluid protein levels, and 3/5 cases were positive for oligoclonal bands. One case had coexisting NMDA receptor antibodies. Brain MRI revealed linear perivascular radial enhancement lesions around the lateral ventricles in 4/5 cases, and one case had a long extensive spinal cord lesion in the thoracic cord. Out of 3/5 cases that underwent cerebral blood flow scintigraphy, 2 cases showed decreased blood flow in the left thalamus. Apathy appears to be not uncommon in GFAP astrocytopathy.

P-5 Exploring B Cell Dynamics through IL-6 Blockade in NMOSD

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Background: IL-6 blockade therapies, including satralizumab, are being used more frequently in clinical practice to treat neuromyelitis optica spectrum disorder (NMOSD). Also, B cells are known to play an important role in the pathophysiology of NMOSD. However, the impact of IL-6 blockade therapy on B cells remains poorly understood.

Objectives: This study aimed to investigate how B cells change over time in patients with NMOSD and explore the effects of IL-6 blockade therapy on B cells. We hypothesized that IL-6 blockade induces regulatory function in B cells, such as producing the anti-inflammatory cytokine IL-10.

Methods: We conducted a longitudinal study tracking B cell subsets in the peripheral blood of patients with NMOSD. Peripheral blood mononuclear cells were stimulated *in vitro,* to promote the expansion of subsets such as double negative B cells (DNs; $CD19^+$ IgD^-, $CD27^-$) and plasmablasts (PBs; $CD19^+$, $CD27^{hi}$, $CD38^{hi}$). After culturing with IL-6 receptor antibodies, whole B cells or B cell subsets were isolated for RT-qPCR to measure *IL10* expression. RNA sequencing of differentiated PBs was performed to identify potential markers of regulatory PBs induced by IL-6 receptor antibodies.

Results: Patients with NMOSD exhibited a higher frequency of DNs and PBs during attacks compared with healthy controls, which gradually decreased along with clinical remission. In the *in vitro* model, IL-6 blockade was found to upregulate *IL10* expression in whole B cells and PBs but not in DNs. RNA sequencing identified *CD200* as one of the differentially expressed upregulated genes in the IL-6 blockade group, suggesting a marker for regulatory PBs. Finally, patients with NMOSD under satralizumab treatment displayed a higher frequency of $CD200^+$ PBs compared with patients in the acute phases.

Conclusions: IL-6 blockade therapy induces a regulatory phenotype in B cells, particularly in PBs. $CD200^+$ PBs may possibly serve as a marker of therapeutic response in NMOSD.

P-6 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-7 Combination Therapy with Ofatumumab and Erenumab in Multiple Sclerosis: A Case Report

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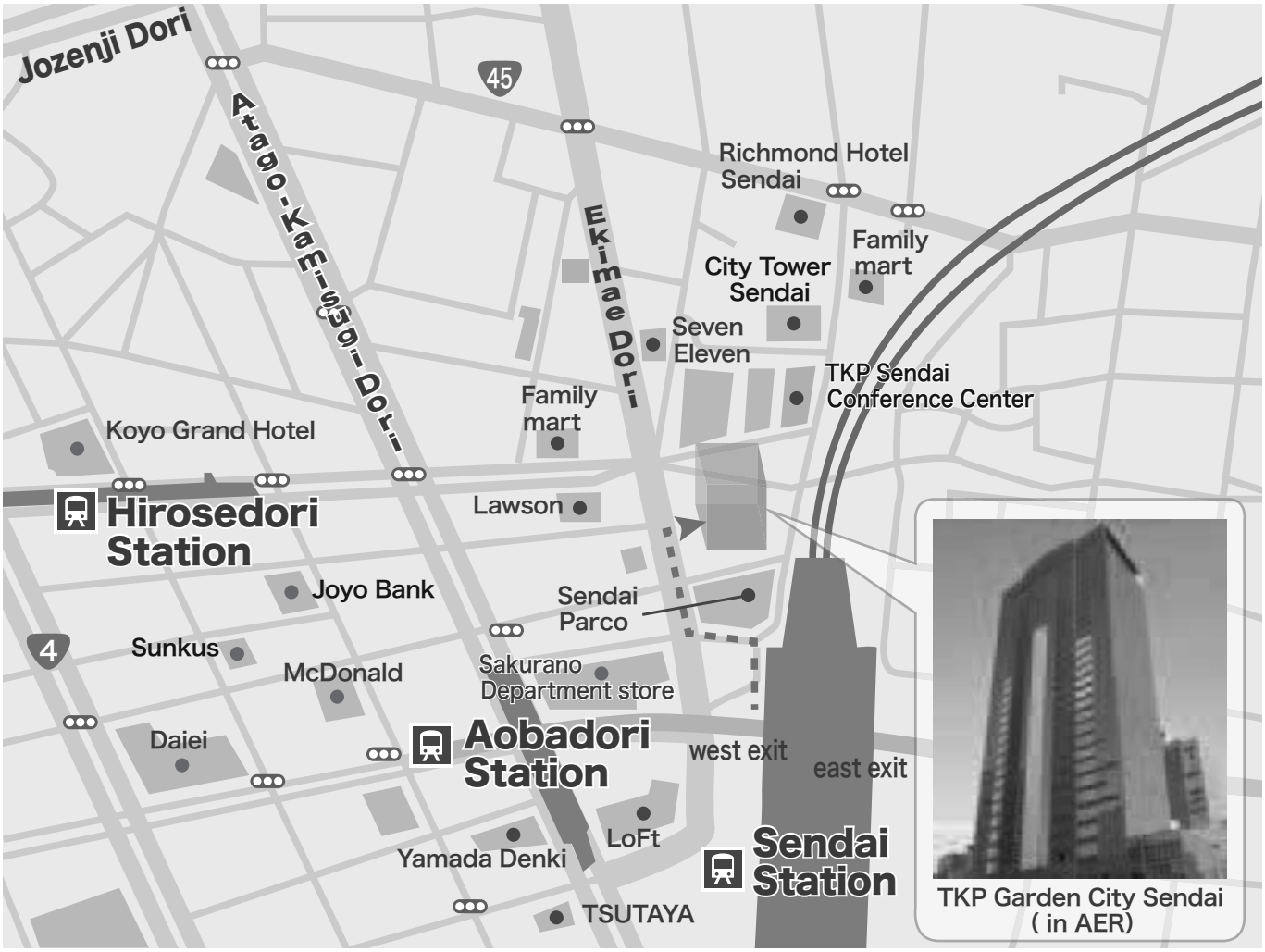
Background: Ofatumumab is a fully human, subcutaneous anti-CD20 monoclonal antibody. While it is utilized as high-efficacy therapy in multiple sclerosis (MS), its safety concerning cutaneous conditions such as pyoderma gangrenosum and its combination with other monoclonal antibodies remain unknown. We aimed to investigate the safety of ofatumumab in patients with cutaneous conditions and its combination with other monoclonal antibodies.

Methods: We report a case with concurrent MS, migraine, and pyoderma gangrenosum who received combination therapy with ofatumumab and erenumab.

Results: A 46-year-old female experienced visual impairment and sensory abnormalities in the limbs since age 40. Diagnosis of MS was based on multifocal white matter lesions in the brain and spinal cord, along with positivity for oligoclonal bands. Additionally, the patient presented with concurrent pyoderma gangrenosum and migraine. She was started on ofatumumab at age 44. At age 45, erenumab was started as a prophylactic therapy, reducing migraine days from approximately 15 per month to about 5 per month without exacerbating multiple sclerosis. Throughout the treatment course, there was no exacerbation of pyoderma gangrenosum.

Conclusions: Ofatumumab can be utilized in an MS patient with pyoderma gangrenosum and migraine, and its combination with erenumab is feasible.

Access



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