Abstract from PACTRIMS

Oral Presentations

Invited Lecture

O-1
Childhood demyelinating disease; lessons for adult disease
Eluen Ann Yeh
Hospital for Sick Children, Canada

Pediatric demyelinating disorders occur in approximately 0.9/100,000 children annually in North America. Approximately half of these children will eventually receive a diagnosis of multiple sclerosis (MS). Research has suggested a longer time to motor disability, but more aggressive disease on MRI and a very high neuropsychological burden in children with MS in comparison with adults with MS. In this talk, clinical features of childhood demyelinating disorders, including acute disseminated encephalomyelitis, optic neuritis, transverse myelitis, and multiple sclerosis will be reviewed, with special attention to similarities and differences with adult disease.

O-2
Demyelinating diseases in a large Neurological center in China: a summary of five year management and follow up
Fu-Dong Shi
Tianjian Medical University, China

We have followed up 245 subjects with demyelinating diseases in our Center in Tianjin, the third largest city in mainland China, since 2008. We evaluated the initial presentation, rate and duration of conversation from clinical isolated syndrome (CIS) to multiple sclerosis (MS) or neuromyelitis optica (NMO). Special attention is paid to 52 NMO patients in terms of their clinical course, with or without other autoimmune manifestations, characteristics of spinal cord lesions, and presence of anti-AQP4 antibodies as well as antibodies to other autoantigens including RF, ANA, SSA, SSB. Coupling with clinical and neuroimaging exams, we critically assessed the responsiveness of NMO patients from our Center to Corticosteroid, Beterseron, Rebif, and Rituximab and compared the efficacy with those of MS patients. We conclude that Chinese NMO patients may have unique clinical and immunological features which warrant more vigorous investigations. We present challenges in the management of these patients due to the limited knowledge about disease characteristics and fewer disease modifying medications that are currently available in China.

O-3
Novel experimental therapies in MS
Jin Nakahara
Keio University, Japan

In the central nervous system (CNS), oligodendrocytes produce myelin. Oligodendrocyte precursor cells (OPCs) are immature and abundant reservoir cells in the adult brain that are capable of differentiating into myelinating oligodendrocytes. Upon demyelination insults, OPCs are spontaneously induced to differentiate to remyelinate demyelinated axons and promote functional recovery. While remyelination is an efficient regenerative process in the normal CNS, it often fails in multiple sclerosis (MS), especially in the chronic phase. Remyelination therapeutic strategy is still poorly developed. Clarification of the mechanism of OPC differentiation as well as understanding the molecular pathology of OPC differentiation arrest in chronic MS shall reveal novel drug targets for the remyelination purpose. From our continuous research, we have elucidated that the gamma chain of immunoglobulin Fc receptors (FcRgamma) is the critical triggering molecule for OPC differentiation, that FcRgamma-stimulating antibodies induce OPC differentiation into myelinating cells (Nakahara et al., Dev Cell (2003)) and provided evidences showing that the molecule is involved in the course of spontaneous remyelination in MS brains (Nakahara et al., J Neuropathol Exp Neurol (2006)). In the current talk, I will summarize aforementioned and related findings and our current research status toward the actual development of remyelination medicines for MS.

O-4
Novel mechanism for MS: implication from basic Neuroimmunology
Akio Suzumura
Nagoya University, Japan

The precise mechanisms of multiple sclerosis (MS) are still unclear, but recent evidences revealed several novel mechanisms in the development of MS pathologies. Here, I introduce new findings related to the effector arms of Th17, and unique mechanism by which effector T cells invade into the CNS. Th17 cells have been shown to play an important
pathogenic role in MS and its animal model, experimental autoimmune encephalomyelitis, but the mechanisms behind this have remained elusive until now. Recent works identify the interleukin-23 (IL-23)/Th17/GM-CSF axis as the major pathway in pathogenesis of autoimmune CNS inflammation. IL-23, a known cytokine that causes autoimmune inflammation of the brain, induces production of more GM-CSF in Th17 cells. GM-CSF is required for the recruitment of inflammatory macrophages to the CNS to initiate EAE. GM-CSF also acts on dendritic cells (DC) to enhance their production of IL-23, which in turn promotes further activation of Th17 cells, GM-CSF production and the perpetuation of chronic inflammation. Like Th17 cells, Th1 cells are dependent on GM-CSF production for initiating EAE, although the mechanisms that drive GM-CSF under Th1 conditions remain unclear. Using EAE models, it has been shown recently that autoreactive T cells access the CNS via the fifth lumbar spinal cord. This location is defined by IL-6 amplifier-dependent upregulation of the chemokine CCL20 in associated dorsal blood vessels, which in turn depends on gravity-induced activation of sensory neurons by the soleus muscle in the leg.

O-5
Novel experimental therapies in NMO
Alan S. Verkman
University of California, San Francisco, USA

Most NMO patients are seropositive for anti-aquaporin-4 immunoglobulin autoantibodies (AQP4-IgG). Current NMO therapies, which have limited efficacy and potential long-term adverse effects, include immunosuppression, immunomodulation and plasmapheresis. There is strong evidence that AQP4-IgG is pathogenic in NMO. AQP4-IgG binding to astrocytes causes complement-dependent cytotoxicity (CDC) and perhaps antibody-dependent cell-mediated cytotoxicity (ADCC), which results in inflammation with prominent granulocyte infiltration and disruption of the blood-brain barrier, with consequent oligodendrocyte death, myelin loss, and neuron death. New therapies for NMO are entering the development pipeline that target specific steps in NMO disease pathogenesis. Because AQP4-IgG binding to AQP4 is likely the initiating event in NMO, we introduced a blocker strategy in which a non-pathogenic antibody or small molecule binds to AQP4, preventing the binding of pathogenic AQP4-IgG. The antibody might be a non-pathogenic, high-affinity monoclonal antibody that is mutated (aquaporumab) or enzymatically modified to eliminate its effector functions. Blockers may be suitable for long-term systemic prophylaxis and acute administration targeting NMO lesions. Other new therapeutic strategies are based on the preponderance of granulocytes in human NMO lesions and experimental evidence supporting their involvement in NMO pathogenesis. The repurposing of approved neutrophil elastase inhibitors and eosinophil stabilizing drugs has promise, particularly for therapy of acute disease exacerbations. Other theoretical possibilities are under consideration for NMO therapy, such as modulators of astrocyte AQP4 expression and supramolecular assembly, and of complement inhibitor expression. The clinical efficacy of these emerging therapies will require human trials.

Main Symposium 1

Cognitive changes in MS: cortical imaging and neural plasticity

O-6
Keynote lecture: Cortical imaging in MSF
Fredrik Barkhof
VU University Medical Center, Netherland

Classically considered as a white matter disease, MRI studies have revived a strong interest in the occurrence of gray matter involvement in MS, with subsequent developments in the field of neuropathology. Since the density of myelin in the cortex is low, neuropathologists need special immunohistochemical stains directed against myelin proteins to visualize cortical plaques, which are a unique feature of MS. Since cortical plaques tend to have little inflammation as well, they are much harder to recognize on MRI. Even with special techniques such as double-inversion recovery (DIR) and imaging at 7 Tesla, the majority of lesion remains undetected. However, since cortical lesions are unique to MS, they convey important diagnostic information, perhaps even more than the juxtacortical lesions currently incorporated in the McDonald criteria. Cortical thinning can reliably be determined using MRI by means of software like FreeSurfer and occurs relatively early in the disease, probably accelerating in the progressive phase. Deep gray matter loss is also observed relatively early in the disease course and relates to alterations in the normal appearing white matter. The hippocampus is another deep gray matter structure that is also typically involved in MS and
contributes to memory loss in MS. In general, GM involvement occurs partly independent from white matter lesions and is an important contributor to clinical impairment, including cognitive impairment.

O-7
Attention deficit in MS
Akitoshi Takeda
Osaka City University, Japan

Introduction: Cognitive decline appears in MS patients in the early stage of the disease and impacts social functioning and employment. Above all, attention deficit may be an important indicator of cognitive decline and may occur in the early stages of MS. Whether Asian MS patients with a low burden of brain lesion have cognitive impairment, similar to MS patients in Western countries, has never been evaluated. We investigated cognitive impairment in Japanese relapsing–remitting MS patients by focusing on attention deficits.

Methods: Twenty-one Japanese patients with relapsing–remitting MS were included in this study. Attention deficits were evaluated using the Clinical Assessment for Attention (CAT) standardized according to age groups. The CAT assesses attention with respect to reaction time, vigilance, short-term storage capacity, mental tracking (working memory), and complex attention. We correlated the deviation between tasks or items. Spearman’s rank correlation coefficient was used to explore correlations between variables.

Results: The completion time for the visual cancellation tasks and/or the reaction times for the continuous performance test were prolonged in 14 patients (66.7%). Response accuracy was preserved throughout the CAT. Deviation from the normal value was not exaggerated according to the increasing difficulty of the task.

Conclusions: Japanese MS patients frequently had attention deficits characterized by slowness of automatic information processing, but controlled processing that requires working memory demands was unaffected.

O-8
Cognitive function test and spectral domain optical coherence tomography in MS and NMO
Etsuji Saji
Niigata University, Japan

Neuromyelitis optica (NMO) is an inflammatory demyelinating syndrome characterized by myelitis and optic neuritis. Recently, it has been reported that cognitive dysfunction and asymptomatic brain lesions were common, and magnetization transfer MRI studies found abnormalities in normal-appearing grey matter in NMO. However, their characteristic features and pathogenesis remain elusive. Therefore, we investigated cognitive dysfunction and evaluated retinal nerve fiber layer (RNFL) thickness as a structural biomarker for axonal loss in NMO spectrum disorders (NMOsd) and multiple sclerosis (MS). Neuropsychological performance was tested using the Rao’s Brief Repeatable Battery (BRBN). RNFL thickness among eyes with (ON eyes) or without a prior history of optic neuritis (non-ON eyes) was measured using optical coherence tomography (OCT). In BRBN assessments, 57% of NMOsd patients and 47% of MS patients had cognitive impairments. In OCT assessments, RNFL thinning occurred in 27% of NMOsd eyes and 30% of MS eyes with non-ON. RNFL thickness in non-ON eyes of NMOsd patients was linked to the scores of symbol digit modality test, paced auditory serial addition test and word list generation controlling for age by a Generalized Estimating Equation model considering within-patient inter-eye relations. These data suggest that cognitive impairments were common in NMOsd and MS, and RNFL thinning in non-ON eyes of NMOsd patients was associated with cognitive impairments.

O-9
Brain atrophy: an in vivo measure of disease activity in MS
Ernst Wilhelm Radue
Medical Image Analysis Center, University Hospital Basel Switzerland

Multiple Sclerosis (MS) is an inflammatory and neurodegenerative disease, which is associated with marked brain atrophy. It occurs early in MS, progresses throughout the course of the disease and affects both gray matter as well as white matter. Advances in MRI techniques and image processing software are improving data quality and allowing new outcome measures, such as whole brain, cerebellar, brainstem, spinal cord and deep gray matter segmentation with acceptable processing times. MR methods for studying global, white matter, but also deep gray matter structures will be discussed with respect to their potential for elucidating specific drug effects (corticosteroids, interferon 1b, monoclonal antibodies, S1P receptor blocker). Measurements of brain atrophy are likely to play an increasing role in MS research and in the diagnosis and staging of the disease as well as for the monitoring of treatment effects.
O-10
Genetic backgrounds for cognitive impairment in MS
Jeannette Lechner-Scott
University of Newcastle, Australia

Recently genetic research in multiple sclerosis has reached a major milestone with the genome wide association study of 20,000 patients with MS. Genes involved in immune activation dominate the list over genes involved with neurodegeneration. None of the therapies based on immunomodulation have been shown to alter the progressive form of the disease. Despite this neurodegeneration is an important factor of the disease course and patients suffer from cognitive impairment and brain atrophy at an early age. None of the genes associated with cognitive impairment in other disorders have shown to be associated with the cognitive impairment in MS. Thorough studies with cognitive assessment over time are warranted to find the genetic bases and ultimately a treatment for cognitive impairment in multiple sclerosis.

Main Symposium 2

A spectrum of NMO and NMOSD in East Asia

O-11
Clinical spectrum of CNS aquaporin-4 autoimmunity with a special reference on influence of pregnancy
Ho Jin Kim
National Cancer Center, Korea

Traditionally, neuromyelitis optica (NMO) was known to involve only the optic nerves and spinal cord. However, the discovery of highly specific anti-aquaporin-4 (AQP4) antibody for NMO enabled us to identify more diverse clinical manifestations. Although the 2006 revised diagnostic criteria mandated optic neuritis (ON) and longitudinally extensive transverse myelitis (LETM) for the diagnosis of NMO, a limited form of NMO, called seropositive isolated LETM or ON, shows similar clinical characteristics and pathology compared with definite NMO. Brain MRI abnormalities in seropositive patients are more common than generally appreciated and are characterized by their unique localization and configuration. Furthermore, not only are symptomatic brain lesions common, but some patients initially present with brain symptoms prior to ON or myelitis. However, studies on the demographic and clinical features of NMO have observed only patients who fulfilled the 1999 or 2006 diagnostic criteria, which mandate two index events with or without restrictive brain lesions. This inclusion of patients according to clinical presentation is limited to show the full spectrum of CNS AQP4 autoimmunity. In this presentation, I will describe the demographic, clinical and prognostic characteristics of anti-AQP4 antibody-positive patients represented by CNS AQP4 autoimmunity. Additionally, I will describe how pregnancy affects the clinical course of NMO, which predominantly affects women of childbearing age.

O-12
AQP4 antibody-sero-positive and sero-negative optic neuritis in China
Xiaojuan Zhang
Tongren Hospital, China

AQP4-Ab positivity is higher in optic neuritis in China, compared with the reports from other countries. In a group of 34 severe optic neuritis patients, the AQP4-Ab positivity was found on 11 (32.4%), and the AQP4-Ab titers of recurrent ON were much higher than those of the single-episode ON. This group of AQP4-Ab sero-positive ON patients had higher female predilection, higher anti-nuclear antibody positivity, much poorer visual outcome and probably higher risk of developing spinal cord lesion than AQP4-Ab sero-negative patients. In a followed-up consecutive optic neuritis study which included 111 cases of immune-mediated optic neuritis, AQP4-Ab was detected in 26(23.4%) cases. Compare with the 85 AQP4-Ab sero-negative patients, the 26 sero-positive patients had much poor visual acuity at the nadir and poorer visual outcome. No significant difference was found regarding brain MRI white matter lesion between AQP4-Ab sero-positive and AQP4-Ab sero-negative groups. During the follow-up time, totally 12 cases(10.8%) further developed into MS or NMO, 7 cases of which were NMO and they all converted from AQP4-Ab sero-positive ON. Meanwhile, the other 5 cases developed into MS were AQP4-Ab sero-negative ON. These outcome further suggested that AQP4-Ab sero-positive ON was more closely correlated with NMO and AQP4-Ab sero-negative ON had closer correlation with MS.

O-13
A large Japanese cohort study for AQP4 antibody-positive cases
Keiko Tanaka
Kanazawa Medical University, Japan

We studied the clinical features of Japanese NMO with large cohort and revealed an extreme predominance in females, a higher onset age, long lesion in the spinal cord (LETM) and severe vision loss as the main clinical features, and a high prevalence of association with other autoimmune diseases. No patients exhibited a progressive course during this observation periods. The initial symptoms of patients with positive-AQP4-ab differed according to age of onset as those younger than 15 exhibited optic neuritis and patients with a higher age of onset tended to exhibit myelitis. Nineteen of the AQP4-ab-negative patients presented with LETM and severe vision loss, which is typical for the NMOSD group. However, further testing revealed that some AQP4-ab-positive or negative patients showed opposite antibody-state during their clinical course due to treatments, disease activity, location of lesions, etc. Furthermore, 57 patients presented initially with cerebrum, brainstem, cerebellum, or their combined lesions. Among them, eight did not exhibit optic neuritis or myelitis during 1 to 5 years of this study. Many brainstem lesions are reported to extend to severe cervical myelitis, but 31 patients from the present study presented with limited brainstem lesions as the initial attack. Appropriate disease preventions are necessary during the early stages of NMO. For the selection of proper treatment regimens as well as the detection of atypical features of NMO, AQP4-ab test is important that sometimes need repetition.

O-14
An expanding spectrum of NMOSD
Ichiro Nakashima
Tohoku University, Japan

Neuromyelitis optica (NMO) is an autoimmune inflammatory disorder with predilection for the optic nerves and spinal cord. Previously considered an uncommon form of multiple sclerosis (MS), evidences from clinical, MRI, pathological and pathophysiological studies over the past decade have convincingly demonstrated that NMO is distinct from MS. In particular, the discovery of NMO-IgG, an NMO-specific autoantibody directed against aquaporin4 (AQP4), a major water channel in the central nervous system (CNS), was a milestone in the NMO research. The term NMO spectrum disorders (NMOSD) also encompasses restricted forms of the disorder which include recurrent optic neuritis (ON), relapsing transverse myelitis (TM), and some encephalitic presentations, and may herald the onset of the disease in patients of all ages. NMOSD are unified by the detection in serum anti-AQP4-antibody. NMOSD include limited forms of NMO (recurrent ON or TM), brainstem disorders, and hypothalamic disorders, which may herald the onset of NMO. In these patients, the absence of the optocospinal phenotype or existence of other clinical features may pose additional diagnostic challenges, and thus anti-AQP4-antibody seropositivity is critical to distinguish them from other diseases.

O-15
A spectrum of NMO and NMOSD in Taiwan
Ching Piao Tsai
Neurological Institute, Taipei Veterans General Hospital, and National Yang-Ming University, Taipei, Taiwan

Retrospective study compared the clinical symptoms, demographics, spinal cord lesion length and AQP4 Ab status of 34 patients with NMO (neuromyelitis optica) with 34 patients diagnosed with conventional MS in Taiwan showed that the NMO patients were predominantly middle-aged women (median age 45 years), exhibited many relapses (1.0/year) and displayed a higher Expanded Disability Status Scale score EDSS (4.75) than conventional MS patients. NMO patients exhibited long spinal cord lesions as detected by MRI. Forty-one percent of the NMO patients had detectable anti-AQP4 Ab. A higher percentage (77.8%) of patients with 34 brainstem NMO had brain lesions with specific NMO patterns, including lesions involving the hypothalamus (n = 6, 33.3%), midbrain or pons (n = 8, 44.4%), periaqueductal regions (n = 5, 27.7%), and medulla (n = 10, 55.6%). Brainstem symptoms/signs and characteristic NMO imaging findings are common in Taiwanese patients with NMO, and should be considered a part of the illness in addition to optic neuritis and myelitis. Long spinal cord lesions with the anti-AQP4 Ab test as well as the brain stem lesions may allow for an earlier diagnosis of NMO and improve therapeutic decisions.

O-16
A tract-based diffusion study of cerebralwhite matter in NMO
Yaou Liu
Capital Medical University, Beijing China
Objective: It remains uncertain whether neuromyelitis optica (NMO) exhibits diffuse cerebral abnormalities or whether the pathology is truly restricted to optic nerves and spinal cord in the majority of cases. We examined NMO patients with diffusion tensor imaging (DTI) and utilized a tract-based spatial statistics (TBSS) method to analyze the data.

Methods: Twenty-seven NMO patients (25 females, age mean ± SD: 35.1 ± 12 years) and 27 age- and sex-matched normal controls were included in this study. Voxel-wise analyses were performed with TBSS using multiple diffusion metrics, including fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (λ1) and radial diffusivity (λ23).

Results: The NMO patients had significantly increased MD (3.6%), λ1 (2.6%) and λ23 (4.6%) in their white matter (WM) skeletons compared with the controls. Furthermore, TBSS analyses revealed significantly (p < 0.05, corrected for multiple comparisons) increased diffusivities (MD, λ1 and λ23) in many cerebral WM tracts in the patients with NMO, including the superior and inferior longitudinal fasciculi, inferior fronto-occipital fasciculi, corpus callosum, cingulum bundles, corticospinal tracts, optic radiation, uncinate fasciculi, fornices, internal capsules, external capsules and cerebral peduncles. Exploratory analyses also revealed the possible associations between WM diffusion changes (MD, λ1 and λ23) and clinical variables (Expanded Disability Status Scale and disease duration) in the patients.

Conclusions: This study provided imaging evidence for widespread cerebral WM abnormalities. While these findings require independent replication, they potentially signify the presence of widespread, low-grade cerebral pathology in NMO.

Main Symposium 3

Molecular Pathology of MS and MS Variants

O-17
Keynote lecture: Recent advances in pathology of MS
Michael Barnett
Australia

The neuropathological interrogation of affected central nervous system tissue has driven multiple sclerosis research for more than 170 years, and in large part shaped concepts of pathogenesis, tissue injury and repair. The relapsing phase of MS is characterised by multifocal inflammatory demyelination that affects both the white matter and grey matter. Although MS is considered to be an organ-specific autoimmune disease, loss of oligodendrocytes in newly-forming lesions is a critical event that may trigger or amplify the inflammatory cascade that characterises active inflammatory demyelination. Recovery from discrete clinical relapses in early disease is mediated primarily by resolution of inflammation and by remyelination, a process that is yet to be fully elucidated at the molecular level. As the disease advances, repair mechanisms progressively fail and the pathological complexity of MS increases. In established disease, clinically relevant neuropathology affects not only the myelin/oligodendrocyte complex, but also axons, neurones, and synapses. Cortical and deep gray matter involvement may be extensive, and correlates best with the cognitive impairment that is frequently observed in progressive disease. Multifocal adaptive inflammation in early disease is replaced by a treatment-resistant diffuse “degenerative” phase, characterised by brain atrophy, neuro-axonal loss and microglial activation. Although inflammation and neurodegeneration are inextricably linked, treatments that target both broad facets of MS neuropathology hold the most promise in preventing the development of irreversible disability.

O-18
Molecular pathology of astrocytopathy in Baló disease and tumefactive MS
Masaki K
Kyushu University, Japan

Demyelinating disease with tumefactive lesions is called Baló’s disease, Marburg’s disease, fulminant multiple sclerosis (MS) or tumefactive MS. These cases are rare and their pathological mechanisms are unclear. Numerous atypical astrocytes (e.g., Creutzfeldt cells) that are positive for glial fibrillary acidic protein and closely associated with oligodendrocytes are characteristic of these conditions. However, very little is known about the precise roles of hypertrophic astrocytes in the pathogenesis of tumefactive lesions. We previously reported extensive loss of aquaporin-4 (AQP4) in Baló’s disease, without perivascular deposition of immunoglobulin or activated complement. However, it is unknown how astrocytopathy induces widespread demyelination. To investigate the relationship between astrocytopathy and demyelination, we focused on connexins (Cxs). Cxs form homotypic or heterotypic gap junctions between astrocytes, or between astrocytes and oligodendrocytes. Astrocytes express Cx43 and Cx30,
while oligodendrocytes express Cx32 and Cx47. In Baló’s lesions, Cx32, Cx32 and Cx47 were extensively diminished in not only demyelinated layers but also preserved myelin layers. At the leading edge of Baló’s lesions, Cx43 and AQP4 loss preceded Cx32/Cx47 loss. Of six Baló’s disease patients, none was positive for anti-Cx43, -Cx32 or -AQP4 antibodies. Some active lesions in tumefactive MS cases also showed loss of Cx43 and AQP4. Loss of AQP4 and Cxs without perivascular deposition of either activated complement or immunoglobulin is characteristic of Baló’s disease and tumefactive MS, suggesting that antibody-independent astrocytopathy may occur in these conditions. Extensive loss of Cxs in tumefactive lesions may contribute to disease pathology by disrupting astrocyte–oligodendrocyte/myelin interactions.

O-19
Role of subarachnoid space as the initiating site for triggering the immune-mediated injury in demyelinating diseases
Izumi Kawachi
Niigata University, Japan

Neuromyelitis optica (NMO) is an inflammatory and demyelinating syndrome characterized by severe attacks of myelitis and optic neuritis. A crucial role for humoral immunity in the NMO pathogenesis has been suggested by the detection of a highly specific serum autoantibody NMO immunoglobulin G that binds to aquaporin-4 (AQP4) water channels, and the pronounced deposition of immunoglobulins colocalizing with products of complement activation in a vasculocentric pattern around thickened hyalinized blood vessels in NMO lesions. Moreover, we have recently demonstrated that levels of several cytokines such as interleukin (IL)-6 and IL-1β are increased in the cerebrospinal fluids of NMO patients, and the demyelinating cord lesions of NMO were accompanied by infiltration of lymphocytes in the leptomeningeal membrane. The cellular elements including T cells in patients with NMO might aid B cells and plasma cells in AQP4 antibody production, and break the blood–brain barrier due to the access of AQP4 antibodies to the extracellular domain of AQP4 at the astrocytic foot process.

Main Symposium 4
Possible pathomechanisms for NMO

O-20
CSF proteomic analysis in MS and NMO
Komori M

Kyoto University, Japan

Multiple sclerosis (MS)-related disorders are inflammatory autoimmune diseases of the central nervous system (CNS). It is important to differentiate these disorders, given their largely overlapping clinical characteristics, and because the optimal treatments for the diseases differ considerably. Neuromyelitis optica (NMO) holds an important position in considering MS-related disorders in East Asia, because of a larger proportion among these disorders. Anti-aquaporin-4 (AQP4) antibody was discovered as a biomarker of NMO. However, a certain number of NMO patients are seronegative for anti-AQP4 antibody and the diagnosis cannot be made solely upon this single marker. It is not clear whether seronegative NMO subjects are the result of inadequate clinical diagnostic criteria, suboptimal assay sensitivity, or different targeted antigens.

The development of mass spectrometry based proteomic approaches prompted us to search for biomarkers in MS-related disorders. We analyzed cerebrospinal fluid (CSF) proteomic patterns from MS-related and non-MS control diseases by using magnetic bead-based enrichment of CSF peptides and proteins followed by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry. Our study reveals distinct CSF proteomic patterns between MS and anti-AQP4 antibody-seropositive NMO. We also succeeded in evaluating and visualizing the similarity of the proteomic pattern between neurological disease groups analyzed. Our findings suggest that CSF proteomic pattern analysis can increase the accuracy of disease diagnosis of MS-related disorders and will aid physicians in appropriate therapeutic decision-making.

O-21
Effects of anti-AQP4 antibody on astrocytes
Nishiyama S

Tohoku University, Japan

Neuromyelitis optica (NMO) is characterized by severe optic neuritis and transverse myelitis. A disease-specific autoantibody against aquaporin (AQP) 4, AQP4 antibody, mainly expressed in astrocytic foot processes, was discovered in the sera of NMO patients. Our pathological study of NMO demonstrated the extensive loss of AQP4 and glial fibrillary acidic protein (GFAP),
especially in the perivascular regions with complement and immunoglobulin depositions. We also reported a marked increase of GFAP in the cerebrospinal fluids during relapse of NMO suggesting astrocytic necrosis. These clinicopathologic data suggest that AQP4 antibody can act on the complement dependent cytotoxicity (CDC) against astrocytes in NMO. Experimental (in-vitro and in-vivo) studies have supported the role of AQP4 antibody in CDC and antibody-dependent cell-mediated cytotoxicity (ADCC). On the other hand, it remains to be elucidated how AQP4 antibody alone can cause morphological and functional changes of astrocytes. These different types of AQP4 antibody-mediated astrocytic damages and their pathogenetic implications will be reviewed.

**O-22**
**Association of AQP4 polymorphism with MS and NMO**
Guangzhi Liu  
*Renming Hospital, China*

Both neuromyelitis optica (NMO) and multiple sclerosis (MS) are inflammatory demyelinating diseases of the central nervous system (CNS). As a specific biomarker, NMO-IgG was recently discovered in serum of NMO patients, followed by a subsequent identification of its target antigen, aquaporin 4 (AQP4). Although the action mechanism of AQP4 antibody (Ab) involved in NMO and MS remains unclear, increasing evidence suggests that AQP-4-related immunology and genetics may have distinct roles in these two CNS disorders. In this study, we analyzed single nucleotide polymorphisms (SNPs) of AQP4 in NMO and MS patients from Chinese Northern Han population to evaluate whether AQP4 SNPs are associated with susceptibility of NMO and MS. Serum of NMO and MS patients were collected and cell-based assay (CBA) was performed to detect the AQP4 Ab. In addition, we genotyped five SNPs (rs1058424, rs3763043, rs335929, rs335931, rs162007), which were selected according to their minor allele frequency in CHB, by high-resolution melting of small amplicons. Our results showed that the association of AQP4 SNPs with Chinese Northern Han MS or NMO was remarkably different from Caucasian population. This may in part lead to the different lesions distribution between the Western and Chinese MS. It is further evidence that AQP4 play an important role in the pathogenesis of NMO.

**Keywords:** Multiple sclerosis, Neuromyelitis optica, Aquaporin 4, Polymorphisms

**Th17 cells and IL-17 gene polymorphism in NMO**
Wang HH

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Our primary research aim is to understand the immunology mechanism of multiple sclerosis (MS) and neuromyelitis optica (NMO). The primary focus is to study whether the novel CD4+T cells like Th17 and their effector cytokines, IL-17 and IL-21 can initiate the inflammatory process in MS and NMO. We have been investigating the peripheral blood Th17 and CD4+CXCR5+T follicular helper cells (Tfh) in MS and NMO patients. We have found increased levels of serum IL-17 and IL-17-secreting T cells in NMO patients, even higher than the levels found in conventional MS (C-MS) patients. We further studied the association of the SNPs in the IL-17 gene with two MS and NMO. We found that IL-17 gene polymorphism may be associated with anti-aquaporin 4 antibody-positive neuromyelitis optica in the Southern Han Chinese. In recent research, we also focus on neurodegenerative pathological features and inflammation-induced endothelial dysfunction in MS and NMO. We found α-synuclein which may reflect the progression of synaptic dysfunction and neuronal apoptosis is higher in MS patients’ CSF and revealed an increased disease disability. We are currently investigating the Pentraxin 3 (PTX3) which is a novel biomarker of inflammatory vascular diseases in MS and NMO. The results are shown plasma PTX3 levels were higher in MS and NMO patients during relapse, and remarkably lower in remission. Several important issues are being addressed: new biologic agents which can inhibition the Th17 differentiation may use to treat animal model of human multiple sclerosis; what mechanisms are lead to injure axons and neurons in inflammatory demyelinating diseases.

**O-24**
**Special Talk from MSIF:**
**Cognitive changes in MS: cortical imaging and neural plasticity**
Peer Baneke

*Multiple Sclerosis International Federation*

**Ordinary Submission**

**Oral Session 1**

**Diagnosis and Immunogenetics of Demyelinating**
Diseases and Mimics

O-25
Evaluation of the McDonald dissemination in space criteria in Korean patients with a clinically isolated syndrome
So-Young, Huh¹; Su-Hyun Kim¹; Woojun Kim²; Sun Ju, Lee¹; Ae-Ran Joung¹; Ho Jin Kim¹
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O-26
Clinical and immunological heterogeneity of optic-spinal multiple sclerosis in China
Jingting Peng¹, Rong Yan¹, Xiuyun Kong¹, Jing Li², Zhenchang Wang³, Xiaojun Zhang³
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O-27
Reappraisal of longitudinally extensive spinal cord lesions by 3 tesla MRI in anti-AQP4 antibody-seropositive and -seronegative NMO and MS patients
Tomomi Yonekawa, Katsuhisa Masaki, Noriko Isobe, Satoshi Yoshimura, Takuya Matsushita, Jun-ichi Kira
Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

O-28
Distribution of Spinal Cord Lesion Length According to Type of CNS Inflammatory Disorders
Ohyun Kwon and Korean MS Investigators Group
Eulji General Hospital, Eulji University College of Medicine

O-29
Relationship Between Human Leukocyte Antigen Polymorphisms and Disease Susceptibility in Japanese Patients with Multiple Sclerosis, Neuromyelitis Optica, or Atopic Myelitis
S. Sato¹; S. Yoshimura¹; T. Yonekawa¹; N. Isobe¹; Y. Kanamori¹; K. Masaki¹; T. Matsushita²; J. Kira¹
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O-30
Non-MS Inflammatory Disorders of the CNS: When, Where and Why?
M Ghadiri, SW Reddel, MH Barnett
Brain and Mind Research Institute, University of Sydney, Sydney, NSW, Australia

O-31
Cerebrospinal fluid levels of IL-21 in multiple sclerosis and neuromyelitis optica
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O-32
Is Vitamin D an Environmental Risk Factor for Neuromyelitis Optica?

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Same as P-94

O-33

Statistical Efficiency of Phase II Multiple Sclerosis Clinical Trials with Different MRI Scanning Frequencies

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Same as P-91

O-34

Early Initiation of Interferon Beta-1b After a First Clinical Event Suggestive of Multiple Sclerosis: Clinical Outcomes and Use of Disease-Modifying Therapy from the BENEFIT Extension Study

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Same as P-92

O-35

B-cell controlled therapy with rituximab

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Same as P-94

O-36

Therapeutic effect of co-administration of Amantadine and Aspirin on fatigue in patients with multiple sclerosis: a randomized placebo-controlled double-blind study

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Same as P-100

Poster Session 1

Epidemiological and Clinical Studies in MS

P-1

Epidemiology of multiple sclerosis in Rafsanjan: South of Iran

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Multiple sclerosis (MS) is the most common disease of the central nervous system that causes permanent disability in young adults. Rafsanjan (south of Iran) is a high-risk area for multiple sclerosis (MS). Objective: To estimate prevalence and other epidemiologic factors in Rafsanjan.

Methods: All patients known to have multiple sclerosis and alive and resident within the chosen area on 15 September 2010 were included in the study. Diagnosis was confirmed by Mac Donald criteria.

Results: A total of 83 patients were identified in this study. MS prevalence was 30 per 100,000. Among the patients 10.9% were male (a female to male ratio of 4:1). The most frequent form of MS was RRMS
(91.3%). Most patients (73.5%) had mild MS. The most common Early symptoms were visual (35%), pyramidal (45/7%), sensory (13/2%) and cerebellar (6.1%).

**Conclusion:** Our data confirm Rafsanjan as a medium-risk area for MS (prevalence rate IS about 50/100,000 in other parts of Iran). We found an unexpectedly high MS prevalence in women.

**P-2**

**Mangalore model of epidemiological survey – A method for establishing minimum prevalence data for multiple sclerosis and allied disorders in resource poor countries.**

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**Background:** In resource poor countries awareness of disease is poor, diagnostic facilities are limited and record keeping is poor. While community based neuro-epidemiological surveys in South India failed to identify demyelinating CNS disorders, a crude prevalence of <1/100,000 was reported for MS, based on hospital acquired data 3 decades ago.

**Objectives:** To determine prevalence and patterns of demyelinating CNS disorders in a well defined and stable population using secure sources, over a one year period.

**Method:** Mangalore, a city in the southwestern coast of India with an area 132.5 sq. km and a population of 419,306 was chosen. Selected specialists and allied health practitioners were sensitized. Registers for minimum patient data entry were placed in private clinics and teaching hospitals which covered the target population. Trained medical social workers collected data regularly. Identified patients were evaluated by L.P for confirmation and characterization of disease.

**Results:** In one survey year, 51 cases were identified. Prevalence rates calculated were MS- 4, NMO-0.9, OPN-3.6, ATM 2.1 and ADEM 0.7/100,000.

**Conclusion:** MS is at least 4 times more prevalent in India than thought before and NMO is not over represented. This survey, besides establishing minimum prevalence data, heightened awareness about a hitherto less known disease locally and sets the background for larger surveys in India.

**P-3**

**The relationship between Epstein-Barr virus infection and multiple sclerosis detected by indirect immunofluorescence assay**

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**Background:** A causal role for virus infection in the pathophysiology of multiple sclerosis (MS) has been suggested and widely debated since the landmark epidemiologic studies. Epstein-Barr Virus (EBV), a human herpes virus has been implicated as both an environmental trigger and as a direct causative agent of CNS immunopathology. In this paper, we will discuss the the EBV in MS patients.

**Objective:** To investigate the infectious conditions of Epstein-Barr virus (EBV) in the patients with multiple sclerosis (MS) by indirect immunofluorescence assay (IFA).

**Method:** In the twenty patients with MS and twenty patients with other neurological diseases (OND), cerebrospinal fluid (CSF) was tested with IFA for anti-EBV capsid antigen (EBV-CA) immunoglobulin G (IgG), IgG affinity of anti-EBV capsid antigen, anti-EBV capsid antigen IgM, anti-EBV early antigen (EBV-EA) IgG and anti-EBV nuclear antigen (EBNA) IgG. According to the CSF antibody patterns, acute infection, chronic infection, primary infection, recurrence of infection and previous infection were compared between these two groups.

**Results:** There was no significant difference in anti-EBV-CA, anti-EBV-EA and anti-EBNA antigen IgG in CSF between MS patients and OND patients (P>0.05). The positive rate of low affinity of anti-EBV-CA IgG in MS patients was significantly higher than that in OND patients (65% vs 40%) (P<0.05). Significant difference in positive rate of anti-EBV-CA IgM was also found between MS and OND patients (75% vs 25%) (P<0.05). 75% of MS patients were on acute stage of EBV infection compared with 40% of OND patients (P<0.05).

**Conclusions:** Acute infection of EBV is common in MS patients.

**P-4**

**Patient-reported Sunlight Exposure in Asian Multiple Sclerosis Patients in China and Canada**

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Background: Global variation in multiple sclerosis (MS) incidence can be ascribed to regional differences in genetic and environmental risk factors, the latter including serum vitamin D status and exposure to solar UV radiation.

Objective: In this pan-Pacific collaboration, we investigate the role of genetic and environmental risk factors in MS susceptibility and prognosis in persons of Asian ancestry by presenting preliminary patient-reported data on sunlight exposure in MS patients seen in China and Canada.

Methods: Patients diagnosed with MS at centres in Shanghai, China and Vancouver, Canada who identified as having full East and/or Southeast Asian ancestry on at least one parental lineage were administered a standardized retrospective questionnaire querying relative sunlight exposure during four age periods: childhood, adolescence, and adulthood, pre- and post-onset. The same questionnaire was administered to a matched cohort of Vancouver patients with northern and/or central European ancestry (Caucasian cohort).

Results: Data on relative sunlight exposure were obtained from 23 Asian and 456 Caucasian cases at the Vancouver clinic, and 47 cases at the Shanghai clinic. Across all 3 cohorts, we observed an upward trend of responses indicating “less than average” sunlight exposure later in life. We also noted a greater proportion of Shanghai cases (34.7-36.7%) reporting “more than average” sunlight exposure during both adult periods compared to Asian cases seen in Vancouver (12.5%).

Conclusions: Preliminary data of observed differences in sunlight exposure between MS cohorts in China and Canada support our ongoing research exploring the relationship between global variation in sunlight exposure and population heterogeneity of MS susceptibility.

P-5
Population Differences in Patient-reported Timing of Onset and Diagnosis in Asian Multiple Sclerosis Patients in China and Canada
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Background: Multiple sclerosis (MS) is a global disease affecting individuals across ethnically diverse populations. Few studies have explored population differences in timing of MS onset and diagnosis.

Objective: The China-Canada MS Study is a pan-Pacific collaboration investigating genetic and environmental risk factors as well as prognostic indicators in Asian MS patients. We examined whether patient-reported age at onset and time to diagnosis differ between MS cohorts in China and Canada.

Methods: MS patients at clinics in Shanghai, China and Vancouver, Canada were administered a standardized questionnaire querying time of MS onset and diagnosis. Patients in Canada were stratified into Asian (east and/or southeast Asian ancestry on at least one parental lineage) and Caucasian (full northern and/or central European ancestry) ethnic cohorts.

Results: Patient-reported age at onset and diagnosis were obtained from 56 Asian and 2,135 Caucasian cases in Canada, and 48 cases in Shanghai. The female-to-male sex ratio was similar across cohorts (range: 2.8-3.3). Females in both the Canadian and Shanghai Asian cohorts reported later age at onset (Canada: 32.5 vs. 27.6 years; China: 35.7 vs. 26.2 years) and time to diagnosis (Canada: 3.0 vs. 1.7 years; China: 2.1 vs. 1.4 years) than males.

Conclusions: Our preliminary data suggest factors associated with ethnicity may underlie sex differences in age at MS onset and time to diagnosis: Asian females may be disinclined to seek medical attention for remitting initial symptoms. It is of specific interest that this trend was observed in both China and Canada, and thus likely does not reflect differential access to medical care.

P-6
MSIF Atlas of MS Database Update: Multiple Sclerosis Resources in the World 2013
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In 2008 the World Health Organization (WHO) and the Multiple Sclerosis International Federation (MSIF) published the report Atlas: Multiple Sclerosis Resources in the World 2008, with the complete dataset made available in the online Atlas of MS Database (http://www.atlasofms.org/). This provided for the first time data on the epidemiology of MS, and the availability and accessibility of resources for people with MS at country, regional, and global levels. MSIF has launched an update program with the intention of publishing the updated database online in October 2013. In addition to updating the data supplied by the 112 countries that responded to the original survey, we hope to obtain data from a further 25 countries, and to improve upon and expand the data collected. For instance, individuals submitting data will be required to cite the data source, which will then be quality rated for its level of evidence.

An online questionnaire has been developed by the Update Coordinator and Update Advisory Group, and a coordinator recruited in each country will identify the individuals and organizations in the country best qualified to complete individual sections of the questionnaire. Received data will be reviewed to ensure consistency with the published literature, organized in themes and presented in charts, maps and text, and published on the Atlas of MS database website.

The updated Atlas of MS will aid the work of health professionals, patient groups, the health industry and governments, inform national and regional advocacy programs, and facilitate policy development to improve outcomes in MS.

**Disclosure/Conflict of Interest:**

This project is funded by the Multiple Sclerosis International Federation.

Peer Baneke has nothing to disclose.

Paul Browne has nothing to disclose.

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Bruce Taylor has no conflicts of interest to declare.

Mario Battaglia has no conflicts of interest to declare.

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Bernard Uitdehaag has received consultation fees from Biogen Idec, Novartis, Merck Serono, Synthony and Danone Research.

Ed Holloway has nothing to disclose.

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**P-7**

**Women and Multiple Sclerosis**

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**Objective:** To study how multiple sclerosis has an impact on various aspects of the life of an Indian woman.

**Methods:** 24 out of 52 women with confirmed diagnosis of multiple sclerosis, attending our MS clinic participated in the study. All patient had to undergo a detailed questionnaire based interview, EDSS examination, serum Vitamin D (25 OH D) and B12 (Cyanocobalamain) levels. The also underwent Paced auditory serial addition test (PASAT), 2 hole peg test and 25 foot timed walk test (25 FTW T) to look at their disabilities.

**Results:** Mean age of our study patients was 32.8 ± 10.9. 24 patients diagnosed as RRMS based on Modified Mc Donalds criteria participated in the study. EDSS ranged from 0-6. Majority 18 (75%) had an EDSS of ≤ = 4.5. 16(66.6%) were graduates and 4(16.6%) professionals. Half of them spoke more than two languages. However in spite of the high education...
majority (70.8%) were unemployed. Among those who were employed 50% had to leave their jobs due to their disability. However their families found it difficult to support them as 58.3% families had an annual income less than rupees one lac (2200 USD). None of the married women in the study were divorced. Childhood infections were seen in 14 (58.5%) Varicella zoster being the commonest (37.5%). The proportion of married woman and their age at marriage were similar to comparable age in the community. However once they were already diagnosed with MS their marriage invariably got delayed. MS patients had smaller family (1.5 child/family) compared to 2.3 child/family in the community. 6 (25%) of our patients had one or more abortions while the abortion rate in general population is 8%. All married woman in our study had at least one living child. None of the children had birth defects and only < 10% was under weight at birth. MS also significantly affected quality of life; with more than half the study patients having depression and anxiety. Insomnia was the most common sleep complaint, impaired sexual arousability and anorgasmia the commonest sexual dysfunction. Those with EDSS ≥ 4.5 performed poorly on 2 Hole peg test and 25 FTWT timed walk test, but there was no correlation between PASAT & EDSS scores. Mean Vitamin D (25 OH D) levels were very low (15.98 ng/ml) in the study group while they had normal Cyanocobalamin level (583.4 pg/ml). Only 4 (16.6%) were on interferons.

Conclusion: Multiple Sclerosis significantly affects the life of women in Kerala.

P-8 (O-25)
Evaluation of the McDonald dissemination in space criteria in Korean patients with a clinically isolated syndrome
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Background: The McDonald criteria based on MRI evidence for dissemination in space (DIS) and time (DIT) has widely used to make early diagnosis of multiple sclerosis (MS) in patients who present with clinically isolated syndrome (CIS). Nevertheless, there have been some debates on applying the McDonald criteria in Asians.

Objective: We aimed to investigate the accuracy of the 2005 and 2010 McDonald DIS criteria for prediction of conversion to MS in Korean patients with CIS suggestive of MS.

Methods: Among the registered patients presented with inflammatory demyelinating diseases of CNS in National Cancer Center, Korea, we excluded the patients whose symptoms were better explained with other disease. Particular attention was made in excluding neuromyelitis optica spectrum disorders (NMOSD), therefore the patients who were seropositive for aquaporin-4 antibody and presented with characteristic features of NMOSD were excluded. Consequently, 69 patients with CIS suggestive of MS, who were followed-up for at least 2 years and whose initial brain MRI was available, were included.

Results: Of 69 patients, 52% converted to clinically definite MS at a median of 13 months from CIS onset. The median age at CIS onset was 32 years and the median disease duration was 45 months. The sensitivity, specificity, accuracy, positive and negative predictive value (%) of the 2005 McDonald DIS criteria were 51.5, 83.3, 68.1, 73.9 and 65.2, while those for 2010 criteria were 69.6, 72.2, 71.0, 69.3 and 72.2, respectively.

Conclusion: After careful exclusion of alternative explanations, the accuracy of the McDonald DIS criteria in Korean patients with CIS suggestive MS was comparable to those observed in Caucasian population.

P-9
The diagnosis status of multiple sclerosis in China
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This paper focuses on the diagnosis of multiple sclerosis in China. We have identified the published researching information from 1976 to 2010 in China. The key issues related to the diagnosis and clinical features of multiple sclerosis in China were summarized. The first patient with MS in China was reported in 1926 from Xiehe hospital. Case reports on MS had been increasing during recent decades. Almost all the patients with MS were confirmed by the McDonald criteria (1977) before 1984. After the year of 1992, even to 2008, the Poser criteria were widely used in China. Although the new diagnostic criteria, McDonald criteria (2001), were presented in 2001, only few papers published in Chinese were reported. After the diagnostic criteria were revised in 2005, McDonald criteria were gradually used in clinical and more and more studies have used the McDonald criteria. This review supported previous observations in Chinese
patients with multiple sclerosis. However, further studies are needed to understand the diagnostic status of MS in China.

P-10
Multiple sclerosis in a series of Sri Lankan patients – Asian or Western?
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Background: Multiple sclerosis (MS) is an immune mediated inflammatory disease which leads to neuronal demyelination in the central nervous system with lesions disseminated in time and space. Studies on MS in Asian populations reveal that the clinical and profile of MS is different from the classical prototypic MS described in the West.

Objectives: This descriptive study aimed to identify the epidemiology, presentations and radiological features and MS patients in Sri Lanka.

Methods: This was carried out as a retrospective cross-sectional study in patients presenting with MS to the Institute of Neurology, National Hospital of Sri Lanka from January 2007 to October 2011. The diagnosis of MS was based on the 2010 revised Mc Donald’s criteria.

Results: The study population consisted of 27 patients. Of these 17 were females (63%). The mean age was 33.8 years. Presentations were; cortical motor deficits = 20, Optic neuritis = 15, cerebellar syndrome = 14, cortical sensory deficits = 11, transverse myelitis = 9, brainstem syndromes = 8. Relapsing and remitting was the commonest pattern of disease (14/27). MRI analysis revealed significant juxtacortical and periventricular involvement.

Conclusions: This study reports the largest series of patients with MS from Sri Lanka. The age and gender distribution, lack of family history and paucity of the progressive subtype was keeping with observations in other regions in Asia. However the clinical and radiological findings observed demonstrated predominance of cortical motor manifestations and optic neuritis. This distribution is similar to that observed in Western countries rather than the optico-spinal distribution observed in Asia. The reasons should be further elucidated.

P-11 (O-26)

Clinical and immunological heterogeneity of optic-spinal multiple sclerosis in China
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Background: Optical spinal multiple sclerosis(OSMS) is common in China. Even it is suggested to be part of neuromyelitis (NMO)spectrum diseases(NMOSD) recently, it is still controversy that OSMS is belonged to MS or NMO.

Objective: To investigate OSMS belonged to MS or NMO.

Methods: The clinical features, brain and spinal cord MRI and some immunological features were retrospectively studied and diagnosed by revised NMO diagnostic criteria.

Results: Totally 66 OSMS patients included. Severe ON was documented on 63 of 124 affected eyes(50.8%) while acute transverse myelitis(ATM) was documented on 27 cases(40.9%). In 61 cases with brain MRI, T2 hyperintense lesions were found in 40 cases (65.6%), of which 5(7.6%) met Barkof’s criteria for dissemination for space, and “NMO-like” brain lesions were found in 7 of 61 cases(11.5%). Hyperintense T2 lesions were found on 45(80.4%) of 56 patients with spinal MRI, including 18(40.0%) cases of longitudinal extensive spinal cord lesions(LESCLs), 6(13.3%) cases of multiple “patchy” lesions and 21 cases(46.7%) of “isolated small lesions”. Aquaporin 4 antibody was positive in 26 of 46 tested patients(56.5%). Thirty-five (53.0%) patients met the revised diagnostic criteria of NMO and were classified as “relapsing NMO” while the 31 cases(47.0%) were kept the diagnosis of OSM. Higher EDSS (3.5±1.5), severe ON(37/61, 60.7%), ATM(19/32, 59.5%) and LESCLs (18/29,62.1%) were statistically more common in relapsing NMO group.

Conclusion: About half of our included OSMS patients met the revised diagnostic of NMO. Clinical, imaging and immunological heterogeneities exist in OSMS patients in China.

P-12
The clinical characteristics multiple sclerosis and neuromyelitis optica patients
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Objectives: Summarize the clinical characteristics of multiple sclerosis (MS) and neuromyelitis optica (NMO) patients in our department; Discuss the key points distinguishing the two diseases.

Methods: The clinical data of MS and NMO patients were retrospectively analyzed; All the data were analyzed by SPSS 16.0. P value <0.05 was considered statistically significant.

Results: The female/male ratio was 1.42 in MS patients, 86.96% of them got first attack during 10-50 years old. The female/male ratio was 8.50 in NMO patients. The media EDSS score of MS and NMO patients were 2 and 4 respectively. Palsy, sensory disorders and ON were the most common symptoms in both groups. More than 50% patients presented isolated nervous symptoms at onset. 26.31% NMO patients presented optical neuritis (ON) and myelitis, 22.81% presented myelitis and 40.35% presented optical neuritis at onset. 80.77% of them presented bilateral ON and 41.96% visual acuity below 0.1. There were 40.22% MS patients presented ON and finally 21.74% MS patients presented bilateral ON. Cerebral and cerebellar symptoms were much more common in MS patients. Only 10.53% NMO patients presented cerebral symptoms.

Conclusion: NMO patients had a higher female/male ratio than MS. The prognosis of NMO was worse than MS. Bilateral ON were more frequently found in NMO patients.

P-13
Diagnostic value of combined testing of AQP4-Ab and ANAs in patients with NMOSDs and MS
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Objective: To investigate the diagnosis value of combined testing of AQP4-Ab and ANAs in patients with neuromyelitis optica spectrum disorders NMOSDs and MS.

Methods: Sixty-five patients with NMOSDs and 45 with MS were screened for serum AQP4-Ab and ANAs simultaneously and enrolled in the study. Sensitivity and specificity of AQP4-Ab, ANAs, combined both AQP4-Ab and ANAs in diagnosis of NMOSDs was calculated and analyzed.

Results: Seroprevalences of AQP4-Ab in NMOSDs and MS patients were 55.4% and 4.4%, respectively. Those of ANAs were 49.2% and 2.2%, and of combined both AQP4-Ab and ANAs were 72.3% and 6.7%. The sensitivity and specificity of AQP4-Ab in diagnosis of NMOSDs were 55.4% and 95.6%, respectively. Those of ANAs were 49.2% and 97.8%, and of combined both AQP4-Ab and ANAs were 72.3% and 93.3%. The sensitivity of parallel test of AQP4-Ab and ANAs in diagnosis of NMOSDs was significantly higher than that of detection of AQP4-Ab (P<0.05) or ANAs (P<0.01) separately.

Conclusion: Combined testing of AQP4-Ab and ANAs can improve the sensitivity in diagnosis of NMOSDs and is valuable for early diagnosis and treatment of NMOSDs.

P-14
Late onset Multiple Sclerosis in far Provinces southern Iran
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Introduction: Multiple sclerosis (MS) is the most common demyelinating and inflammatory disease of central nervous system. After trauma multiple sclerosis is the most common cause of neurological disability in young adults, but in a subgroup of patients the first clinical symptoms presented after age 50 years. This late clinical presentation is defined as late onset multiple sclerosis (LOMS). The incidence and prevalence of MS including LOMS varies geographically. The aim of this study is to determine epidemiological characteristic of late onset MS in southern Iran.

Patients and Methods: All patients with age over 50 year old and known to have definite Multiple Sclerosis according to MC Donald’s criteria, and were members of Shiraz University Multiple Sclerosis Database (SUMSD) were evaluated in this study.

Results: From 1705 patients with clinically definite Multiple Sclerosis or CIS (clinically isolated syndrome), 138 patients (7.2%) identified as late onset M.S (time at onset of presentation over 50 years) which 60 patients (3.1%) identified as very late onset MS (VLOMS). Mean age of the patients with LOMS at the time of diagnosis was 58.81 years (with SD 2.6 year and 95% C.I 57.5 – 59.6). The oldest patient had 72 years old. 31 patient (20.8%) were male and 107 (79.2%) were female with female to male ratio of 3.4. 89.1 % of patients received Beta interferon as a disease modifying treatment including Avonex (16.3 %) cinovex (32.6%) Rebif (14.1%) and Betaferon (26.1%).
Discussion: LOMS is a subgroup of MS that is not rare in south of Iran (Fars province). Incidence rate of 1-6 % was reported in some studies in other countries. In our study 7.2 % of all MS patients identified as LOMS. In this subgroup clinical history and para clinical data should be thoroughly evaluated to exclude more common conditions like cerebro vascular disease.

P-15
Clinical features in children with multiple sclerosis
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Objectives: To improve diagnosis of multiple sclerosis by analyzing the characteristics of clinical presentation, magnetic resonance imaging (MRI) , Electroencephalogram (EEG) , oligoclonal bands in CSF and visual evoked potential (VEP) in children with MS. Methods The medical records of 24 MS patients were analyzed by retrospective analysis. Results 24 MS patients (16 relapsing-remitting cases and 8 secondary-progressive cases) were included. There were 8 males and 16 females, the M: F ratio was 1:2. All cases were acute or sub-acute onset with various initial presentation including visual loss(12 cases), cortical symptoms (8 cases with seizures, consciousness disturbance, memory deterioration, etc), paralysis and numbness(4 cases). Fever was present in 6 cases. First diagnosed ADEM (9 cases) or viral encephalitis(2 cases). Brain MRI showed typical multifocal lesions in 21 cases. Periventricular and callositas were involved most frequently. As to spinal cord injury, 9 patients were checked, only three patients suffered cervical spinal cord injury or cervical-thoracic spinal cord joint injury. VEP were performed in 20 MS patients. The abnormality rates of VEP were 100%. EEG were performed in 9 patients, only 1 was normal. The other 8 cases showed slow brain wave, some even showed spike wave. CSF check was performed in 8 patients. It showed positive oligoclonal bands in 3 patients. Conclusions Childhood MS possesses some manifestations different from those of adults, which play an important role in the diagnosis of MS. [Key words] child ; multiple sclerosis ; initial presentation ; accessory examination

Sclerosis?
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Introduction: Multiple sclerosis (MS) is the most frequent chronic autoimmune demyelinating disease of the central nervous system (CNS). Purpose of this study is to determine the relationship between the site of cervical disk herniation and cervical spinal cord plaque in our outpatient’s clinic for MS patients, Shiraz, Iran.

Methods: All patients with definite diagnosis of multiple sclerosis at our outpatient clinic, Shiraz, Iran; from Sept. 2004 to Sept. 2011, which were 536, were involved in this prospective study. All patients underwent cervical MRI for primary investigation of the disease .The patients with cervical cord lesion, 471 patients, were selected and their MRIs were evaluated for detection of any site of cervical disk herniation. Any correlation between the site of lesion and disk herniation was recorded.

Results: Over all 536 patients were involved in the study, 441 (82.3%) of the patients were females and others were males. Mean age of the patients was 28.2 years. Disk herniation was seen in 214 (40.9%) of the patients. 148 (28.3% of the all patients) had cervical plaque at the same site of cervical disk herniation. In 66 patients cervical plaque and disk herniation didn’t have any correlation regarding the site of the lesion. The number of patients with plaque and herniation at same site was significantly higher than those with these lesions at different sites (p < 0.05).

Discussion: With regards to these facts, it is possible to consider a relation between cervical disk herniation and cervical MS plaque.

P-17
Clinical And Radiological Characteristics Of Tumefactive Demyelinating Lesions: Follow-up Study
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1-7
Background: Demyelinating lesions over 20 mm in size, referred to as tumefactive demyelinating lesions (TDLs), can be misdiagnosed as being either a tumor or an abscess. Although some radiological characteristics help to make a differential diagnosis between multiple sclerosis (MS) and the other etiologies, cerebral biopsy may be necessary.

Objective: We aimed to assess the clinical and radiological characteristics of TDLs, and present follow-up data for 54 patients with TDLs.

Methods: Demographic, clinical, radiological and laboratory data were gathered and treatment responses were evaluated in a total of 54 patients from five MS centers.

Results: Twenty-nine patients out of 54 were diagnosed with TDLs at onset, whereas in 25 patients, TDLs developed after a diagnosis of MS. Median follow-up was 38.12 months. Nineteen of the patients with TDL at onset, developed relapsing–remitting MS, while 10 remained as a clinically isolated syndrome. The tumefactive lesions were mostly focal, with closed-ring enhancement. Oligoclonal band positivity was less frequent in the patients with tumefactive onset.

Conclusion: The distribution of the patients’ clinical course differed from formerly reported demographical characteristics of Turkish MS population. There was an absence of primary progressive MS and a lower frequency of secondary progressive MS cases in our study group. The less frequent oligoclonal band positivity and the difference in the clinical course in our study group suggest that further studies are needed to compare all the biological and immunological differences between classical MS and TDLs, in order to reveal whether there are different pathogenetic mechanisms involved.

P-18

Relationship between Lower Extremity Strength and Balance in patients with Multiple Sclerosis

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Background: Limited number of studies showed that relationship between lower extremity muscle strength and balance in patients with Multiple Sclerosis (MS).

Objectives: The purposes of this study were to investigate the relationships between the lower extremity strength and standing balance in patients with MS.

Material and Method: Forty-four patients with MS (mean age: 37.30±8.52 years, mean Expanded Disability Status Scale: 1.80±1.13) and 10 healthy subjects (33.9±5.78) were included to the study. Lower extremity muscle strength (hip flexion-extension-abduction-adduction, knee flexion-extension, and ankle dorsal flexion) were assessed by using a hand held dynamometer (Baseline®). Balance was measured as duration of one leg standing using with a digital chronometer.

Results: Lower extremity muscle strength and duration of one leg standing balance were decreased in patients with MS when compared with healthy controls (p<0.05). All lower extremity muscles (hip flexor, extensor, abductor, adductor, knee flexor, extensor, and ankle dorsal flexors) strength was found related with duration of one leg standing in patients with MS (p<0.05).

Conclusions: These results indicate that the lower extremity muscle strength and duration of one leg standing balance were decreased in MS patients. Lower extremity strength seems to be related with one leg standing balance. Therapies contains lower extremity strengthening may contribute to balance in patients with MS.

P-19

The Preparatory Study of the Rehabilitation Exercise Sets for the Patients with Multiple Sclerosis

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Research background: Multiple Sclerosis (MS), an inflammatory demyelinating disease of the central nervous system, usually has high disability rate. Because of its complexity, variety, long-duration, progression, unpredictability, and lower incidence, it is hard to find the effective rehabilitation treatments. Most professional rehabilitation agencies lack experiences with the MS. The patients with MS often feel challengeable to pursue long-term therapies in those agencies due to their financial deficiency. Therefore, the rehabilitation mode, which is patient-centered and home-based, has been proved and recognized as an effective interference. The domestic and foreign literatures show that at present, for the patients with MS, the rehabilitation exercises at home are almost the
same as those in the professional agencies, such as balance training, resistance training, cycle ergometer training, and etc; there isn’t any specifically designed home-based rehabilitation exercise sets for the patients with MS, which is simple, effective, sequencing, easy to learn and persist. This study developed a MS Exercise Set according to the MS characterizes and principles of MS exercise rehabilitation. 

**Research purpose:** To develop a set of rehabilitation exercises for the MS; to tentatively test the efficiency of the rehabilitation exercises set by the clinical practice.

**Research method:** The experimental subjects are the patients with relapsing-remitting MS, who are stable during the test. The subjects were classified as experimental group(10 cases) and control group(43 cases). The patients in experimental group practiced the MS Exercise Set, and the control group were guided with the normal MS education. The test duration was 1 month. The EDSS was used as assessment before and after the test. Use the software SPSS19 to do the t-test of the corresponding paired samples, t-test of two samples.

**Research result:** 1. Before the experiment, there was no statistics difference of the gender (P=0.428), age (P=0.554), and function level (P=0.284) of the patients between the experimental group and the control group. 2. The EDSS score of the control group before the experiment was no statistics difference with the one after the experiment (P=1.000). 3. The EDSS score of the experimental group before the experiment had significant difference (P=0.003) with the one after the experiment.

**Research conclusion:** The rehabilitation exercise sets is helpful for the MS. It can improve the function of the MS.

**P-20**

Seizure among Iranian patients with multiple sclerosis  
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**Background:** Several studies show a high seizure activity risk among patients with multiple sclerosis (MS).

**Objective:** In this study, seizure and its characteristics analyzed among patients with MS.

**Patients and Methods:** We reviewed the medical records of all definite multiple sclerosis patients referred to the Kashani hospital, Isfahan, Iran, between 2007–2011.

**Results:** Altogether, 34 cases with seizure activity identified among the 920 definite MS patients (3.69%). Five excluded due to the other probable etiologies rather than MS. In the remained 29 patients (3.15%), type of seizure was mostly generalized (79.3%); interictal electroencephalography showed an abnormal pattern in 84.6%, brain magnetic resonance imaging revealed subcortical white matter lesions in 84.6% of patients, the mean duration of multiple sclerosis onset was 8.17 years. In general, response to antiepileptic treatment was excellent.

**Conclusion:** The prevalence of seizure among MS patients is higher than the general population. The subcortical plaques may explain the seizure activity in multiple sclerosis.

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Nocturia in Multiple Sclerosis: A Pilot Study  
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**Background:** Nocturia is a common symptom in multiple sclerosis (MS). One possible mechanism is that autonomic dysfunction blunts the normal overnight reduction in blood pressure (BP), increasing nocturnal urine production. This research was aimed at studying patterns of nocturia in MS patients and its relationship to nocturnal blood pressure (BP) and heart rate (HR).

**Method:** Consecutive ambulatory MS patients were screened for nocturia before being asked to participate in the study. Urine production was measured by self-completed diary, and 24-hour ambulatory BP and HR were measured by ambulatory recording (CardXplore). Results were compared with sex matched controls of similar age (age 41±14.4 years).

**Results:** Amongst 30 ambulatory MS patients, 18 (60%) reported nocturia of ≥1/night, and 10 consented to the study. There were 5 females and 5 males, aged 43.1±9.3 yrs (mean ± SD), with EDSS ranging from 2-5. Patients who self-reported nocturia did have demonstrable increased nocturnal urinary frequency. Compared to controls, the study group had more frequent nocturia (1.6 vs. 0.1, p=0.008), and passed both a larger proportion (36.3% vs. 28.2%, p=0.009) and total volume (656 vs 414ml, p=0.04) of urine at night. MS patients also had smaller urine volumes both during day (149 vs 210ml, p=0.05) and night (246 vs 410ml, p=0.01). Ambulatory BP and HR did not differ between the study group and controls.

**Conclusion:** Nocturia in ambulatory MS patients
occurs in the context of higher nocturnal urine production. This does not appear to be related to higher BP and HR overnight.

**P-22**

**Cardiovascular Involvement in Relapsing Multiple Sclerosis: Does Course of the Disease Have Any Effect?**

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**Background and Objective:** Ventricular repolarization dysfunction has been reported as one of the cardiovascular manifestations of autonomic dysfunction in MS. However, there is no study investigating the effect of course of the disease in cardiovascular abnormalities in relapsing MS. QTc (i.e., heart rate corrected QT) and QT dispersion (QTd) are non invasive reliable parameters useful in assessing homogeneity of cardiac depolarization and autonomic function.

**Methods and Materials:** QT, QTc and QTd were measured by means of a standard surface 12-lead electrocardiograph in 35 RRMS patients in relapse phase, 35 sex- and age-matched MS patients in remission and 35 healthy controls. Ventricular repolarization dysfunction was evaluated between these 3 groups looking for relationship between QTc and QTd abnormalities and phase of the disease in relapsing MS and was compared to a control group.

**Results:** QT interval was significantly different between 3 groups (p=0.016), but when corrected for the heart rate it didn’t reach the level of significance (p=0.907). QT dispersion was impaired (>70 ms) in 6% of patients in relapse, compared to 3% of those in remission. However, it didn’t reach the level of significance comparing 3 groups (p=0.654). No significant correlation was observed between QTc/QTd and disease activity (based on EDSS score).

**Conclusions:** Course of the disease seem to have no effect on QTc and QTd abnormalities in patients with relapsing MS. However, sporadic abnormalities still are more frequent in relapse than in remission. Concerning probability of cardiac involvement, ECG evaluation for every relapsing MS patient may be recommended.

**Poster Session 2**

**Clinical Studies in NMO and MS Mimics**

**P-23**

**Aquaporin-4 antibodies in Korean patients with idiopathic inflammatory demyelinating diseases of the central nervous system**

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**Objective:** To evaluate the diagnostic utility of aquaporin-4 antibodies (AQP4-Ab) for idiopathic inflammatory demyelinating diseases (IIDDs) of the central nervous system in Korea.

**Methods:** In total, 153 consecutive patients with IIDDs from three major hospitals in Korea were included. All were tested for AQP4-Ab using a cell-based assay at the John Radcliffe Hospital, Oxford, UK. Patients were evaluated for neuromyelitis optica (NMO), other NMO spectrum disorder (OTHER NMOSD), and multiple sclerosis (MS).

**Results:** Fourteen patients fulfilled the criteria for NMO, 64 were identified as OTHER NMOSD, 25 fulfilled the criteria for MS and 50 had either CIS or topographically restricted IIDD. Patients with NMO required a mean follow-up duration of 37.3 month before experiencing both optic neuritis and myelitis. AQP4-Ab test positivity in patients with OTHER NMOSD was only 21.9%. About 40% of patients with limited manifestations of NMO would have fulfilled the 2010 International panel criteria for MS, without the antibody test results.
Conclusions: The AQP4-Ab assay can be crucial in the differential diagnosis of IIDDs in Koreans, because it facilitated the early diagnosis of most NMOs, showed low positivity in Korean patients with OTHER NMOSD, could prevent limited NMO patients from being misdiagnosed with MS. In addition, because some IIDD patients who did not have features of NMO or OTHER NMOSD can show the positive test results, clinical suspicion for the atypical manifestation of NMO or aquaporinopathy is needed.

P-24
Detection of Anti-Aquaporin 4 Antibodies in the Neuromyelitis Optica Spectrum Diseases
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Objective: To establish an immunofluorescence assay to test the aquaporin-4 (AQP-4) antibodies and evaluate its clinical significance for NMO patients.

Methods: AQP-4 antibodies were measured in sera from 153 patients of central nervous system inflammatory demyelinating disease using cell-based immunofluorescence assay (CBA). The clinical information of the patients were analyzed.

Results: (1) The sensitivity and specificity of the assay for NMO patients is 83.3% and 100%, respectively. (2) AQP4 Antibody-positive rate of female NMO patients was 88.6% and the positive rate of male was 28.6% (P <0.05); The NMO patients who had AQP4 antibodies combined with other systemic autoimmune disease antibodies, the EDSS score at the disease onset was 5.9 ± 2.0, higher than those NMO patients only detected out AQP-4 antibodies, 4.2 ± 1.9 (P <0.05); no correlation was seen between AQP-4 Abs score and the clinical indicators such as the EDSS score of the disease onset, disease year recurrence rate, length of the spinal cord lesion on MRI, and brain abnormality; serum AQP4 Abs was positive in the acute/relapse phase while negative in the remission period, and immunosuppressant treatment could reduce the serum AQP-4 antibodies level, even to be difficult to test out.

Conclusion: The CBA assay can be used as a high sensitive and specific detection method; Aquaporin-4 is a major and differential diagnostic marker for neuromyelitis optica, and conductive to evaluate the relapse of the NMO spectrum diseases.

NMO-IgG Status In Neuromyelitis Optica And Related Disorders In An Indian Cohort: Our Experience
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Background: Neuromyelitis optica (NMO) is an immune-mediated inflammatory demyelinating disorder of the central nervous system with a striking predilection for the optic nerves and the spinal cord. Immunopathological evidence suggests that the target antigen of the disease is aquaporin-4, a water channel. An immunoglobulin G (IgG) antibody to this protein has been explored as a molecular marker for the disease and has shown promise as a diagnostic tool due to its high sensitivity and specificity, in various populations.

Objective: To examine NMO-IgG seropositivity in Indian subjects with demyelinating disorders.

Methods: 45 patients with clinical and magnetic resonance imaging features consistent with demyelinating disorders were evaluated for the presence of serum NMO-IgG (anti-aquaporin-4 antibody) by indirect immunofluorescence assay using the EUROIMMUN kit (Lubeck, Germany). Of these patients, 21 patients satisfied Wingerchuk’s criteria for NMO, and 12 patients belonged to the NMO spectrum disorders. 12 patients satisfied McDonald criteria for multiple sclerosis (MS).

Results: Of the 21 patients satisfying the criteria for NMO, 17 showed seropositivity (80.9%), and of the 12 belonging to the NMO spectrum disorders, 6 showed seropositivity (50%). None of the 12 patients satisfying McDonald criteria for MS showed NMO-IgG seropositivity. Sensitivity and specificity of the assay were 80.9% and 100% respectively (excluding the patients having NMO spectrum disorder).

Conclusions: NMO-IgG, in this study, shows a high seropositivity in NMO and related disorders in Indian patients, which is comparable with seropositivity rates seen in Western and other Asian populations.

P-26
The Spectrum of Neuromyelitis Optica
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Background: Neuromyelitis optica (NMO) is an idiopathic inflammatory demyelinating disease of the central nervous system with a predilection for the optic nerves and spinal cord with positive anti-aquaporin 4 antibody.

Objective: To review the clinical features of our patients who tested positive for anti-aquaporin 4 antibody.

Methods: Patients referred to our clinic with positive anti-aquaporin 4 antibody were reviewed.

Results: We reviewed 4 patients who had a history of transverse myelitis. 2 had a history of optic neuritis. Of these 2, both had recurrent myelitis and optic neuritis and were treated as mixed connective tissue disease and multiple sclerosis respectively. The remainder 2 had first onset transverse myelitis as their sole clinical finding. None were diagnosed as neuromyelitis optica initially. All patients had longitudinally extensive transverse myelitis (LETM) on MRI. All 4 tested positive for anti-aquaporin 4 antibody. All patients had their diagnoses revised. 2 had definite NMO while the rest were classified as NMO Spectrum Disorder (NMOSD) as they did not meet the criteria for definitive NMO.

Conclusions: All patients with longitudinally extensive transverse myelitis should be tested for anti-aquaporin 4 antibody.

P-27
PRELIMINARY DATA FROM THE ANZ NMO COLLABORATION
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Background: Neuromyelitis optica (NMO) is a severe demyelinating illness which typically affects the optic nerves and spinal cord. The recent discovery of an autoantibody directed against aquaporin-4 (NMO IgG) has led to a significant rethink with regards to the pathophysiology and clinical presentation of this disease.

Objective: This study aimed to delineate the clinical and serological features of NMO in a cohort of clinically defined cases from across Australia and New Zealand (ANZ).

Methods: Clinical and MRI data were collected from clinically suspected NMO cases and age/sex matched multiple sclerosis (MS) cases. NMO IgG testing was conducted at a single laboratory using standard immunofluorescence techniques.

Results: To date 145 referrals have been received, the present data relate to the first 27 suspected cases of NMO and 15 MS cases with complete data. The median age (range) for NMO was 42 (15 – 68) and MS was 47 (25 – 68). The proportion of females was 23/27 (85%) for NMO and 11/15 (73%) for MS. Cases with NMO were more severely affected than MS (mean EDSS 4.0 vs 2.8). Wingerchuk 2006 criteria were met in 18/27 suspected NMO cases and of these 10/18 (55%) were positive for NMO IgG (sensitivity = 55%). None of the MS cases were positive for NMO IgG (specificity = 100%).

Conclusions: NMO in Australia occurs predominantly in Caucasians. The Female: Male ratio for NMO is higher than for MS. The sensitivity for NMO IgG is lower than generally previously published (55%) but the test is specific.

P-28
THE NATURAL HISTORY OF NEUROMYELITIS OPTICA IN BRAZILIAN PATIENTS
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We describe here the natural history of a recently recognized idiopathic inflammatory disease, neuromyelitis optica with recurrent clinical course.

Method: we analyzed the clinical course, morbidity and mortality in a cohort made of all patients that fulfilled the diagnostic criteria of NMO (2008) followed between 1986 and 2012 in Hospital da Lagoa (Rio de Janeiro).

Results: Among 153 patients with NMO syndrome, 109 patients were selected for the study. 90.8% women, 70.6% African-Brazilians. The mean age of onset was 31,28 years (sd 14,01, 5-70 years). AQP4 antibody was positive in 61%. The first event was optic neuritis - 47,7% [unilateral 26,6%, bilateral 21,1%] myelitis - 43,2% [complete 34,9%; partial 8,3%], optic-spinal - 1,8%, brainstem syndrome - 5,5% and encephalopathy - 1,8%. The median time between the index events (NO/MT) was of 9,5 months (range 1 day-268 months). At nadir severe visual impairment occurred in at least one eye in 88,9% of the patients and severe motor dysfunction in 48,6%. After a mean time of disease of 10,19 years (sd 8,01, range 1-35) 789 acute events were observed (61% myelitis, 25 % optic neuritis, 6 % optic-spinal, 5 % brainstem syndrome and 3% encephalopathy). Brainstem syndrome occurred in 16 patients and cerebral involvement with encephalopathy in 10. At last follow up, 92,7% of the patients had severe visual dysfunction (61,4% bilateral and 31,3% unilateral) and 58,7%, severe motor dysfunction (7
P-29

Analysis correlative factors in clinically isolated syndrome conversion to neuromyelitis optica

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Objective To explore influential factors for the evolvement from Clinically isolated syndrome (CIS) into optic nerve myelitis (NMO). Methods One hundred and nine patients with clinical isolated syndrome (CIS) were included in author hospital form Sep, 2004 to Nov, 2011. All of the patients were retrospectively analyzed first head and spinal cord MRI characteristics and clinical manifestation. 30 healthy subjects’ serum were collected as normal control group. Serum Aquaporin-4 antibody (AQP4-Ab) level was detected with Enzyme-linked Immunosorbent Assay (ELISA). According to optical density (OD) and standard curve, antibody concentration was calculated. Results (1) All patients were followed-up for the mean of 4.3 years (range 0.5 to 7 years), of whom 46 and 29 respectively had developed into NMO and MS, the remaining had been still classified as CIS. (2) The AQP4-Ab level of serum in conversion to NMO group patients was significantly higher than patients in the other groups (MS group, TM group, ON group) and normal control group (P< 0.05). (3) AQP4-Ab positive rate in conversion to NMO was 63% (29/46), which was higher than the rate of conversion to MS group 13.8% (4/29), TM group 41.2% (7/17), ON group 25% (2/8), and there were statistically significant difference (P< 0.05). (4) Multi-factor analysis indicated that AQP4-Ab positive, NMO brain typical lesions, longitudinal spinal lesions and EDSS were correlated with CIS conversion to NMO. Conclusion AQP4-Ab positive, NMO brain typical lesions or typical spinal cord injury more than three segments, EDSS are valuable to predict CIS conversion to NMO. AQP4-Ab detection rate by ELISA and the currently accepted cell indirect immunofluorescence assay is closed. ELISA is appropriate in clinical promotion, which needs lower the requirements of the experimental techniques and cost.

P-30

Analyses of Influential Factors to Quality of Life in Patients with Neuromyelitis Optica

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Objective: To explore the influential factors to quality of life in patients with neuromyelitis optica (NMO). Methods: Retrospective study was carried out to study the inpatients with NMO in Shanghai sixth hospital from March 1995 to May 2012. The neurological function of 36 diagnosed NMO patients were evaluated by Activities of Daily Living (ADL) scale at discharge. The influential factors of related disablement were analyzed with unvaried analysis and multivariate logistic regression analysis. Result: There were 36 (10 male and 26 female) patients with NMO in our study. Disease duration, age at onset, time to definite NMO, the location and length of the lesions in the spinal cord could not predict the prognosis. Variables of gender (OR: 1.039, 95% CI: 1.005-1.078), number of attacks (OR: 1.078, 95% CI: 1.014-1.164) and the presence of Aqp-4-Ab (OR: 2.529, 95% CI: 1.050-5.836) were left in the final model of multivariate logistic regression analysis for associations with the severity of disability. Conclusion: Female, more episodes and the presence of Aqp-4-Ab were significantly associated with a more severe disability. Further longitudinal investigations are needed to evaluate the prognosis of patients with NMO in China.

P-31

AQP4-IgG detection and the clinical analysis of Chinese patients with neuromyelitis optica

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Neuromyelitis optica (NMO) predominantly affects the optic nerve and spinal cord and is difficult to be distinguished with multiple sclerosis (MS). AQP4-IgG is considered as a common useful serological marker of NMO, but the crucial pathogenic role of AQP4-IgG in NMO remains yet unproven. To understand the characters of Chinese NMO patients with AQP4-IgG, we retrospectively evaluated the clinical presentations of 45 NMO cases, including MRI of brain and spinal cord, detection of serum AQP4-IgG...
and some auto-antibodies, and cerebrospinal fluid (CSF) analysis. NMO was prevalent in women at the mean age of 41.8±14.3 years. 66.7% patients were AQP4-IgG-positive, 82.2% and 26.7% presented with longitudinally extensive spinal cord lesions (LESCLs) and brain lesions respectively, 24.4% had other auto-antibodies; In CSF analysis of twenty-eight patients, 57.1% were with pleocytosis, 14.3% patients had oligoclonal bands (OBs) while 25% and 53.6% showed large IgG Index and increased albumin quotient respectively. There were no statistically significant differences about demographic, clinical and imaging features of AQP4-IgG-positive and -negative patients. AQP4-IgG is prevalent in Chinese NMO patients, but AQP4-IgG-positive and -negative NMO cases seem to have about the same clinical and laboratory presentations.

P-32
Role of aquaporin-4 antibodies in Chinese patients with neuromyelitis optica: a 2-year follow-up study
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Abstract: We determined the presence of aquaporin-4 (AQP4) antibodies by indirect immunofluorescence in human AQP4-transfected cells, and evaluated the diagnostic and prognostic relevance of AQP4 antibodies in 210 Chinese patients with neuromyelitis optica (NMO), high-risk (HR)-NMO, classic multiple sclerosis (MS), and other neurologic diseases. Patients were enrolled from The General Hospital of the Chinese People’s Liberation Army and followed up for a median of 2 years. The patients with HR-NMO had optico-spinal MS (OSMS; n=3), longitudinally extensive transverse myelitis (LETM; n=35), recurrent optic neuritis (n=2), optic neuritis (ON) with Sjögren’s syndrome (n=1) and transverse myelitis (TM) positive for SSA antibodies (n=1). The sensitivity and specificity of AQP4 antibody in NMO were 70.9% and 91%, respectively. The median AQP4 antibody titer was significantly higher in patients with NMO (1:320) than that in HR-NMO (1:100) and MS (1:50). Relapse of ON or TM was more likely in patients with seropositive than seronegative HR-NMO. Among AQP4 antibody-seropositive patients, 66.7% (36/55) had severe ON, 75.9% (41/55) had TM, and 55.6% (30/55) had spinal cord lesions longer than 3 segments, while ON and TM relapsed in 14.8% (8/55) and 35.2% (19/55) of patients, respectively, during the 2-year follow-up.

In conclusion, our study revealed that AQP4 antibody is a sensitive and specific biomarker for discrimination of NMO, classic MS, and other neurological diseases, and is particularly useful for the diagnosis of HR-NMO. AQP4 antibody-positive patients showed higher frequencies of relapse of ON or TM compared with AQP4 antibody-negative patients.

P-33
Associated Factors with Activities of Daily Living in Chinese Patients with Neuromyelitis Optica
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Objective: To explore associated factors with Activities of Daily Living (ADL) in Chinese patients with neuromyelitis optica (NMO).

Methods: ADL was examined at discharge and a number of putatively associated factors were investigated for consecutively hospitalized patients with NMO in Shanghai Sixth Hospital during the period from March 1995 to May 2012. Unvaried analysis and multivariate logistic regression analysis were performed to analyze the association between the factors and ADL.

Results: There were 10 male and 26 female inpatients with NMO in our study. No significant associations were found between disease duration, age at onset, time to the diagnosis of NMO, location and length of the lesions in the spinal cord and ADL. Variables of gender, number of attacks and Aqp-4 Ab were left in the final model of multivariate logistic regression analysis, and female (OR: 1.039, 95% CI: 1.005–1.078), number of attacks equal to x times or more (OR: 1.078, 95% CI: 1.014–1.164) and presence of Aqp-4 Ab (OR: 2.529, 95% CI: 1.050–5.836) were significantly associated with more severe disabilities.

Conclusion: Female, episodes equal to x times or more, and presence of Aqp-4 Ab were significantly associated with a more severe disability in patients with NMO. Further longitudinal investigations are needed to evaluate the prognostic value of the associated factors in patients with NMO in China.

P-34
Neuromyelitis Optica and Pregnancy
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Background: Neuromyelitis Optica (NMO) is a rare but severe disease affecting young adults with a mean age at onset of 34.5 years. The female: male ratio is 9:1 in Asian, so most of patients are women of childbearing potential. They will ask clinician for risk of pregnancy but very few data are available. Objective: The aim of this study was to precise the clinical course of NMO during and after pregnancy.

Methods: We performed an observational study. Data were collected from The Third Affiliated Hospital of Sun Yet-sen University. We calculated the annualized relapse rate (ARR) for the year before pregnancy, during each trimester of pregnancy and for the first and the second trimester post partum.

Results: The study is still progressing. Conclusion: From the data already collected, we conclude that pregnancy influences the activity of NMO.

P-35
Clinical Features and Prognosis of neuromyelitis optica in pediatric patients (13 case reports)
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Objectives: To analysis the clinical characteristics, imaging features, and specificity of aquaporin water channel antibody (NMO-IgG) and prognosis of NMO in pediatric patients. Clinical manifestations of NMO patients are various. In order to reflect this diversity, the term of NMO spectrum have been proposed.

Methods: The medical records of 13 NMO children patients were studied by retrospective analysis. Their the average age was 11 years old. The Wingerchuck standard was used as diagnostic criteria.

Results: All children had visual acuity loss in both eyes simultaneously or successively, and showed transverse spinal cord injury in the disease course. Brain MRI of six cases in the early onset showed abnormal lesions, however, only four cases had related symptoms caused by those lesions. NMO-IgG-positive rate was 77%.

MRI showed that seven cases had lesions located in the cervical spinal cord, four cases in the thoracic spinal cord, three cases in both neck and thoracic spinal cord, the length of spinal cord lesion ≥3 vertebral segments in eight cases, brain lesions in six cases. The average recurrent episodes of each patient is four in this group, in which two cases had legacy mild functional disability, two cases had severe functional disability, three cases were recovered after treatment.

Conclusion: The optic nerve is most vulnerable to be damaged in NMO children. Brain MRI findings are distinct from the MS patients, NMO-IgG also shows positive in children with NMO.

The most number of children NMO is relapsing form, which is more common in female. The main clinical manifestations are bilateral optic nerve injury and long-segment myelitis, and some patients show brain lesions in early onset. Children NMO spectrum disease is mostly monophasic and with a high risk of relapse, and has a better prognosis.

P-36
Clinical, radiographic features and immunomodulating changes in neuromyelitis optica with extensive brain lesions
**equally contributed

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Purpose: To investigate clinical, radiographic features and immunomodulating changes of neuromyelitis optica (NMO) with extensive brain lesions (EBLs) in China.

Methods: Clinical features, magnetic resonance imaging (MRI) scans, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and complement (including C3, C4, CH50) levels of 16 NMO patients with EBLs and 53 NMO patients without EBLs from January 2006 to February 2010 were retrospectively analyzed. All the patients were with 2 years visit of follow-up.

Results: The EBLs of MRI features were divided into five types: 1. Tumefacive-like lesions; 2. ADEM-like lesions; 3. MS-like lesions; 4. PRES-like lesions; 5. The shape cannot be defined. The patients with EBLs had higher AQP4 seropositive rate, higher rate of encephalopathy symptoms and homonymous hemianopia, higher EDSS scores. In the last visit of 2 years follow-up, the EDSS scores were higher in patients with EBLs. Immunomodulating changes (such as C3, C4, ESR, and CRP) were significantly higher in the patients with EBLs. Significant positive correlations were found in NMO patients with EBLs between the mean EDSS levels and serum CRP (r=0.529, p=0.02) and ESR(r=0.725, p=0.002).
Conclusions: Clinical symptoms of brain involvement and the MRI characteristics of NMO with EBLs, the presence of EBLs in NMO could reflect higher disease activity and portend a worse prognosis. CRP is useful for monitoring disease activity, systemic inflammation is a key component of forming EBLs in NMO and emphasizes early initiation of disease modifying, anti-inflammatory therapy of NMO with EBLs.

P-37
Correlation of neuropathic pain and spinal cord magnetic resonance imaging findings in neuromyelitis optica patients
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Background: Neuropathic pain is often experienced by multiple sclerosis (MS) patients. However, the occurrence of neuropathic pain in neuromyelitis optica (NMO) patients is less well studied.
Objective: To assess the clinical characteristics of neuropathic pain in NMO patients, and analyze the relationship between the length of spinal cord lesions and neuropathic pain severity.
Methods: Thirty-five patients with NMO and 15 with MS were analyzed retrospectively. DN4 and ID pain questionnaires were used to assess neuropathic pain. Clinical data and spinal cord MRI findings for all NMO patients were analyzed.
Results: Neuropathic pain was more severe in NMO patients than in MS patients. In all, 82.9% of NMO patients had DN4 scores ≥4, compared with only 46.2% of MS patients (p=0.017). Numbness, hypoesthesia to touch, and hypoesthesia to prick were the most common symptoms in NMO patients. Pain most commonly occurred in the lower limbs (85.7%), upper limbs (42.9%) and head (37.1%, including eye pain) in NMO patients. DN4 scores were correlated with spinal cord length in NMO-IgG-seropositive NMO patients (r=0.394, p=0.046).
Conclusions: Neuropathic pain is more severe and frequent in NMO patients than MS patients. Neuropathic pain scores may be correlated with spinal cord lesion length in NMO-IgG-seropositive NMO patients.

P-38
Intractable Pruritus in Neuromyelitis Optica and Neuromyelitis Optica Spectrum Disorders
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Background: It has been found that neuromyelitis optica (NMO) or NMO spectrum disorders (NMOSD) was an entity disease which is different from MS. Paroxysmal symptoms such as pruritus were often reported in patients with MS, but rarely reported in NMO or NMOSD.
Objective: To investigate the clinical characteristics of pruritus in NMO and NMOSD, and explore the underlying mechanisms.
Methods: A retrospective review of NMO cases and NMOSD between 2009 and 2011 from the Demyelinating Disease Database in Third Hospital of Sun Yat-sen University was done. All medical notes with documented “pruritus” or “itching” were extensively studied.
Results: 18 NMO-IgG sero-positive NMO patients (18/64) and one NMOSD patient (1/15) had pruritus prior to, accompanying, or after onset of optica neuritis (ON) or transverse myelitis (TM). With exception of two patients, all were female. The median age of symptom onset was 38 years (range, 19-66). The median disease duration was 15 months (range, 0-72). Six patients complained of onset symptoms that included pruritus, accompanied with or without impaired vision or limb weakness. Eight patients complained of pain at the pruritus areas when touched. The pruritus areas Correlated with innervated skin segments of the affected cord lesions in six NMO patients. However, for the other twelve NMO patients, the itching areas were smaller than, or even without correlation to, dermational distribution of cord lesion level. All 19 patients exhibited pruritus at time of relapse, with no pruritus during remission. 18 NMO patients exhibited extensive, longitudinal spinal cord lesions. A total of 13 presented with brain lesions, 10 had lesions in the brain stem, and four had lesions in the periaqueduct gray matter. All NMO patients presented with dorsal horn lesions in the spinal cord. However, the NMOSD patient presented with no lesion in the spinal cord, but an obvious lesion in the periaqueduct gray matter. Compared to previous MRI scans, newly formed and enhanced lesions were detected in all patients, either in the brain or spinal cord.
Conclusion: Pruritus is far more common than
P-39

Pleocytosis Is Rare In the Cerebrospinal Fluid of Anti-Aquaporin4 Antibody Positive Neuromyelitis Optica.
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Background: The original Wingerchuk’s diagnostic criteria for neuromyelitis optica (NMO) in 1999 included cerebrospinal fluid (CSF) pleocytosis of >50 white blood cells (WBC)/μl or >5 neutrophils/μl. Given anti-aquaporin4 (AQP4) antibody in 2006, it was revised: Pleocytosis was excluded, and anti-AQP4 antibody was included.

Objective: To validate the exclusion of pleocytosis from the revised criteria.

Methods: Five cases of NMO with anti-AQP4 antibody were studied. Neurological status, expected spinal lesions, and CSF findings (WBC count, IgG, protein) were evaluated in 34 attacks in these cases. Correlations between the WBC count and other parameters were also analyzed.

Results: The disease onset was 37 to 64 years of age. CSF pleocytosis (>50 WBC/μl) was found in one attack (2.9%). The WBC count for the rest was as follows: 0~4 cells/μl in 19 (56%), 5~9 in 10 (29%), 10~14 in 2 (5.9%), >15 in 2 (5.9%). Pleocytosis of >5 neutrophils/μl was found in one attack (2.9%). The counts (mean ± standard deviation) of WBC, lymphocytes, and neutrophils were 6.7±11.0/μl, 6.1±10.2/μl, and 0.5±1.2/μl, respectively. CSF protein was 41.3±14.0 mg/dl and IgG was 5.7±2.6 mg/dl. On average, spinal lesions spanned the length of 3.3±1.5 vertebral bodies. No significant correlation was found between WBC count and protein, IgG, and spinal lesion length.

Conclusion: CSF pleocytosis is relatively rare in NMO, supporting the exclusion of it from the revised diagnostic criteria.

Factors associated with the AQP4-Ab positivity in patients with longitudinally extensive transverse myelitis (LETM): possible role of asymptomatic VEP abnormality.
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Objective: To evaluate the factors associated with the aquaporin-4 antibodies (AQP4-Ab) positivities in patients having isolated longitudinally extensive transverse myelitis (iLETM) without optic neuritis in Asian population.

Methods: Fifty patients with iLETM, who did not meet the criteria for definite NMO and did not have a symptoms of optic neuritis, were included from three major hospitals in Korea. All were tested for AQP4-Ab using a cell-based assay at the John Radcliffe Hospital, Oxford, UK.

Factors as gender, age, Kurtzke extended disability status scale (EDSS) at nadir, EDSS ≥ 6 after intravenous methylprednisolone (IVMP) treatment for acute relapse, visual evoked potential (VEP) abnormality without symptoms of optic neuritis, radiologic characteristics, and other laboratory characteristics were assessed.

Results: Of 50 patients with isolated LETM, 9 (18%) showed positive AQP4-Ab test results. Asymptomatic VEP abnormality, poor response to acute IVMP treatment, severe disability at relapse, as well as female gender and relapsing disease course were significantly associated with AQP4-Ab positive test results in patients with LETM. However, age of onset, presence of asymptomatic brain lesion, maximal length of spinal cord involvements, and cerebrospinal pleocytosis were not associated with the AQP4-Ab test results.

Conclusions: A considerable number of patients with AQP4-Ab-positive LETM who did not have recognizable optic symptoms might have sub-clinical optic nerve involvement, which could facilitate the early diagnosis of definite NMO. In addition, the presence of AQP4-Ab in LETM patients may assist prediction of long-term prognosis, disability at acute attack, and the need for a second-line acute-phase treatment.

P-40

Previously, believed, and could be a characteristic feature for NMO and NMOSD.

P-41 (O-32)
Is Vitamin D an Environmental Risk Factor for Neuromyelitis Optica?
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Background: No study has so far compared serum 25-hydroxy vitamin D (25(OH)D) concentration in neuromyelitis optica(NMO) patients and normal population.

Objective: We measured level of 25(OH)D in NMO patients and compared it with healthy controls to answer the question whether or not vitamin D is an environmental risk factor for NMO.

Methods: In this cross-sectional study, A total of 29 NMO patients and 39 age and sex matched healthy individuals were enrolled from August to September 2011. We compared the mean level of 25(OH)D in the two groups and searched for a probable correlation between 25(OH)D serum concentration and NMO features through statistical analysis.

Results: Mean level of 25(OH)D in NMO patients was significantly higher than in the controls (34.75 vs 16.16ng/ml, p<0.001). No relationships between vitamin D concentration and progression index(p=0.185), NMO IgG seropositivity(p=0.19), relapse rate(p=0.12) and presence(p=0.77) and location of longitudinally extensive transverse myelitis in the MRI images(p=0.07), were found.

Conclusions: Our findings suggest that vitamin D does not appear to be an environmental risk factor for NMO. This implies that at least some pathophysiologic aspects of NMO may be different from those of Multiple Sclerosis.

P42
Is NMO Related To Pulmonary Tuberculosis?
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Background: Neuromyelitis optica (Devic’s disease) is an inflammatory, demyelinating syndrome of the central nervous system that is characterized by severe attacks of optic neuritis and myelitis. Although a number of case reports have described the presence of PTB in patients diagnosed with NMO, a definite association between the two conditions was not conclusively demonstrated.

Objective: To investigate whether PTB is associated to NMO.

Methods: We performed a retrospective review of hospital records of consecutive patients admitted to our hospital with a diagnosis of NMO (including NMO spectrums) and other neurological diseases (OND) from January 1, 1995 to December 31, 2011.

Results: 105 patients with NMO were enrolled in our study. The frequency of preceding/simultaneous PTB in NMO patients showed no significantly difference compared with OND groups (P > 0.05) except cryptococcus meningitis/encephalitis (P = 0.005) and tuberculous meningitis/encephalitis group (P < 0.001). NMO-IgG were only detected in the NMO patient, not in patients with OND despite of preceding PTB. NMO patient with PTB showed no CSF or radiological findings suggestive of TB infection in central nerve system.

Conclusion: Present study did not confirm previous speculation on the association of PTB and NMO.

P-43
Seronegative LETM in Korean Males; is it related with toxocariasis?
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Background: Longitudinal extensive transverse myelitis (LETM) is defined as a spinal cord lesion that extends over three or more vertebrae. Whilst LETM is a classically associated with NMO, there are many other causes. Clinical and laboratory characteristics of LETM in Korea remain to be elucidated.

Methods: We retrospectively reviewed medical records and spinal MRIs of 59 Korean patients who were diagnosed with LETM. All patients completed test for anti-aquaporin4 antibody (AQP4-Ab) using cell-based indirect immunofluorescence assay. We compared clinical, laboratory and radiological features between patients with AQP4-Ab-positive and negative LETM.

Results: Among 59 patients with LETM, 33 (56%) were seropositive for AQP4-Ab and 26 (42%) were male. Seronegative group showed a male predominance compared with seropositive patients (male to female, 8:25 vs 18:8; 69.2% vs 24.2%, p=0.001) and relatively
shorter involvement of spinal cord (4.8±3.1 vs 9.2±5.5, p=0.000). Toxocara canis antibodies were more frequently observed in seronegative group than seropositive (15/26 vs. 2/32, p=0.000), whereas autoimmune antibodies were more frequently detected in seropositive group (66.7% vs 30.8%, p=0.006).

**Conclusion:** We should consider other causes beside NMO in seronegative Korean male patients with LETM. Toxocarasis may be considered as one of the important etiologies.

**P-44 Clinical Implications of Positive Serum Anti-TES Antibody in Transverse Myelitis Patients**
MH Choi, YH Hong, IS Joo

**Department of Neurology, Ajou University School of Medicine, Suwon, Korea**

**Background:** Although toxocara myelitis is known to be rare, toxocarasis is still considered as one of the differential diagnoses for transverse myelitis(TM) and the serologic test directed against Toxocara excretory-secretory antigen (TES Ag) by ELISA method is commonly used.

**Objective:** We aimed to clarify the role of seropositivity against TES Ag in supporting the diagnosis of toxocara myelitis.

**Methods:** We compared the clinical and laboratory data of 1) 57 TM patients with those of 100 control patients and 2) 17 seropositive TM patients with those of 28 seronegative TM patients, to see any significant effects that could be related to the seropositivity.

**Results:** In comparison with the control group, the TM group did not show any significant difference in seroprevalence and hypereosinophilia status. In addition, the seropositive TM group did not make any significant difference in seroprevalence, hypereosinophilia status, neurological disability at initial presentation and follow-up period, compared to the seronegative TM group.

**Conclusions:** Seropositivity against TES antigen alone is not a sufficiently reliable marker for the diagnosis of toxocara myelitis. To strengthen the causal relationship, other complementary tests (CSF Ab titer, IgE titer, etc.) also should be included in the diagnostic workup.

**P-45 (O-30) Non-MS Inflammatory Disorders of the CNS: When, Where and Why?**
M Ghadiri, SW Reddel, MH Barnett

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**Background:** Despite the broad spectrum of identifiable central nervous system (CNS) inflammatory disorders other than multiple sclerosis (MS), individual conditions are relatively rare. Distinguishing these disorders from MS is imperative to avoid potentially harmful MS treatment and permit appropriate directed therapies.

**Objective:** We examined the spectrum of non-MS CNS inflammatory disease seen at a university-based, neuroimmunology-focussed outpatient practice to determine how these conditions are best differentiated from MS. We explored clinical and neuroradiological patterns in patients with CNS inflammatory disease of uncertain aetiology.

**Methods:** We searched the clinical records of 10,000 consecutive patients seen at the Brain and Mind Research Institute between 2005 and 2012. Patients with any immune-mediated CNS disease other than MS were identified and their clinical features, laboratory results and magnetic resonance imaging were reviewed. Patients with MS, a clinically isolated syndrome likely representing first presentation of MS, non-immune CNS disease or bland micro-vascular ischaemic disease were excluded.

**Results:** Eighty patients with immune-mediated CNS inflammation were identified. The clinical, neuroradiological and laboratory features permitted a definite or probable diagnosis to be reached in 68 of these cases. Atypical features and patterns alerting the clinician to specific diagnoses in these cases are discussed. No aetiology was established in 12 cases.

**Conclusions:** Despite the scope of non-MS CNS inflammatory disease, analysis of disease patterns often permits accurate diagnosis. However, a minority of cases do not conform to recognisable patterns and elude specific diagnosis. Pooling data on such cases may help identify new disease entities and inform treatment decisions.

**Poster Session 3**

**Imaging Study in NMO**

**P-46 (O-27) Reappraisal of longitudinally extensive spinal cord lesions by 3 tesla MRI in anti-AQP4 antibody-seropositive and -seronegative NMO and MS patients**
Tomomi Yonekawa, Katsuhisa Masaki, Noriko Isobe, Satoshi Yoshimura, Takuya Matsushita, Jun-ichi Kira
Longitudinally extensive transverse myelitis (LETM) has recently gained much attention as an indicator of CNS aquaporin-4 (AQP4) autoimmunity and been incorporated as a supportive criteria for the diagnosis of neuromyelitis optica (NMO). We analyzed data of Korean Multiple Sclerosis Registry to determine the distribution of spinal cord lesion length and to find out whether LETM works as a valid indicator for AQP4 autoimmunity in this patient cohort.

Among the patients enlisted on Korean Multiple Sclerosis Registry, ones with radiologically confirmed spinal cord lesion were categorized to one of the followings: clinically isolated syndrome (CIS), MS, NMO, acute disseminated encephalomyelopathy, and other autoimmune CNS inflammatory disease. And the spinal cord lesion length was compared according to the type of disorder and AQP4 seropositivity.

Out of total 597 patients enlisted (M: F=1:1.71, onset age, 37.3±14.4 years, disease duration, 4.9±11.6 years) in the registry, 413 patients (69.2%) had at least one episode of myelitis. Among them, the results of AQP4 seropositivity were available in 273 patients (66.1%). Longitudinally extensive spinal cord lesions (LESCLs) were significantly associated with negative AQP4 antibody (odds ratio 3.23, p<.001). The length of spinal cord lesion in AQP4 antibody seronegative group was 5.9±4.3 vertebral segments (VSs) which was 2.4 VSs longer than that of AQP4 seopositive group (p<.001) and this tendency was kept even in clinically isolated syndrome and neuromyelitis optica subgroups.

This result contrasts the widely accepted notion that LESCL be indicative of AQP4 seropositivity, at least in this Korean Cohort. Other yet unrevealed or underrecognized etiology of LESCL in AQP4 seronegative patients group should be sought to explain this paradox.

Background: Neuromyelitis optica (NMO), more common in Asia, is different for multiple sclerosis (MS) in many aspects including clinical manifestation, pathology, MRI findings and treatment response to interferon-beta. The diversity of MRI lesions in MS or...
Neuromyelitis optica (NMO) is an inflammatory condition characterized by the selective involvement of the optic nerves and spinal cord. The finding of aquaporin-4-antibody (AQP4-Ab, or NMO-IgG) indicates that NMO is a different disease from MS. Magnetic Resonance Spectroscopy (MRS) has been used to analyse the metabolite status of brain tissue. The MRS study on brain lesion and NAWM in MS patients indicates that there is diffuse metabolite change in the whole brain of MS patients. And some researches find that NMO patients have brain atrophy even at early stage of the disease. However, diffuse white matter change and brain atrophy is absent in NMO patient.

Objective: Explore MRS characteristics and atrophy degree of NMO patients and find more differences between NMO and MS.

Subjects and methods: We retrospectively analyze the clinical datas, MRI and MRS findings of brain lesion and NAWM, and the brain atrophy degree for all the NMO and MS cases between 2009 and 2011 from the Demyelinating Disease Database in Third Hospital of Sun Yat-sen University. And compare the degree of brain atrophy between NMO and MS. The brain atrophy is estimated by linear atrophy markers, which is intercaudate ratio (ICR).

Results: Compared to the brain lesions of MS patients, the NAA/Cr of the lesions in NMO patients is higher, the Cho/Cr and mI/Cr in NMO patients is lower (P<0.05). Compared to the NAWM of MS patients, the NAA/Cr of the NAWM in NMO patients is higher, the Cho/Cr and mI/Cr in NMO patients is lower (P<0.05). The ICR of NMO patients is smaller than that of MS patients (ICR\textsubscript{NMO}=0.1077±0.0027, ICR\textsubscript{MS}=0.1274±0.0280, P<0.05). There is no correlation between MRS characteristics and brain atrophy degree of NMO patients (P>0.05).

Conclusions: There is pathophysiologic changes in normal appearing white matter of NMO patients. But MRS can’t differentiate NMO from MS. And the atrophy degree of NMO patients is milder than that in MS patients.

P-49
The Study on Clinical and Magnetic Resonance Spectroscopy Characteristics of Neuromyelitis Optica
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Background: Neuromyelitis optica (NMO) is an inflammatory condition characterized by the selective involvement of the optic nerves and spinal cord. The finding of aquaporin-4-antibody (AQP4-Ab, or NMO-IgG) indicates that NMO is a different disease from MS. Magnetic Resonance Spectroscopy (MRS) has been used to analyse the metabolite status of brain tissue. The MRS study on brain lesion and NAWM in MS patients indicates that there is diffuse metabolite change in the whole brain of MS patients. And some researches find that NMO patients have brain atrophy even at early stage of the disease. However, diffuse white matter change and brain atrophy is absent in NMO patient.

Objective: Explore MRS characteristics and atrophy degree of NMO patients and find more differences between NMO and MS.

Methods: Patients with NMO having at least two relapses in spinal cord were included fulfilling Wingerchuck revised criteria (2006). All cases were given spinal and brain MRI scanning, evoked potentials, CSF OB, and serum AQP-4 Ab.

Results: One hundred fifty one patients (female: 83; male: 68) were included. The relapse was from 2 to 6. Forty-five patients (29.8%) had positive CSF OB. Serum AQP-4 Ab was positive in 72 cases (47.7%). Total spinal lesions were 397. The recurrent spinal lesions at the same segments were 319 (80.4%), while those at the different location were 78 (19.6%).

Conclusions: The majority of spinal lesions on MRI in NMO reappear in the same spinal segments when relapsing. The pathogenesis of this finding needs to be further investigated.

P-50
Altered Topological Organization Of White Matter Structural Networks In Patients With Neuromyelitis Optica
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Background: Neuromyelitis optica (NMO) is an inflammatory, demyelinating syndrome of the central nervous system characterized by severe attacks of optic neuritis and myelitis. Imaging evidence of brain abnormalities in NMO has been demonstrated by several recent studies, challenging the notion of spinal cord and optic nerve restricted pathology in NMO. However, it is unknown whether these abnormalities are significant enough to alter the brain anatomical connectional architecture.

Objective: In this study, the distribution features of spinal lesions on MRI in NMO are analyzed. The brain atrophy between NMO and MS. The brain atrophy is estimated by linear atrophy markers, which is intercaudate ratio (ICR).

Methods: Patients with NMO having at least two relapses referring to the first attack both in MS and NMO.

Results: One hundred fifty one patients (female: 83; male: 68) were included. The relapse was from 2 to 6. Forty-five patients (29.8%) had positive CSF OB. Serum AQP-4 Ab was positive in 72 cases (47.7%). Total spinal lesions were 397. The recurrent spinal lesions at the same segments were 319 (80.4%), while those at the different location were 78 (19.6%).

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P-49
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Results: Compared to the brain lesions of MS patients, the NAA/Cr of the lesions in NMO patients is higher, the Cho/Cr and mI/Cr in NMO patients is lower (P<0.05). Compared to the NAWM of MS patients, the NAA/Cr of the NAWM in NMO patients is higher, the Cho/Cr and mI/Cr in NMO patients is lower (P<0.05). The ICR of NMO patients is smaller than that of MS patients (ICR\textsubscript{NMO}=0.1077±0.0027, ICR\textsubscript{MS}=0.1274±0.0280, P<0.05). There is no correlation between MRS characteristics and brain atrophy degree of NMO patients (P>0.05).

Conclusions: There is pathophysiologic changes in normal appearing white matter of NMO patients. But MRS can’t differentiate NMO from MS. And the atrophy degree of NMO patients is milder than that in MS patients.
Objective: To investigate the topological alterations of whole-brain white-matter (WM) structural networks in patients with NMO.  

Methods: The present study involved 26 NMO patients and 26 age and sex-matched healthy controls (HC). WM structural connectivity in each participant was imaged with diffusion-weighted MRI and represented in terms of a connectivity matrix using a deterministic tractography method. Graph theory-based analyses were then performed for the characterization of brain network properties. A multiple linear regression analysis was performed on each network metric to compare NMO and HC groups.  

Results: The NMO patients exhibited abnormal small-world network properties, as indicated by increased normalized characteristic path length, increased normalized clustering and increased small-worldness. Furthermore, largely similar hub distributions of the WM structural networks were observed between NMO and HC. However, regional efficiency in several brain areas of NMO patients was significantly reduced, mainly in the default-mode, sensorimotor and visual systems.  

Conclusion: Although NMO patients in this study had no discernible white matter T2 lesions in the brain, the disrupted topological organization of cerebral WM networks provides additional evidence for subtle, widespread cerebral WM pathology in NMO.

P-51  
Study of MR diffusion tensor imaging and the  
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Objective: we will study the correlation between DTI and VEP, and OCT in the neuromyelitis optica. It means that we study the correlation between DTI parameters and the latency of P100, and the retinal nerve fiber layer thickness quantitatively. Object and methods 20 NMO patients are screened stringently under the criteria of inclusion and exclusion in the out-patients or in-patients in our hospital. At the same time, we choose 20 healthy cases matched in age and sex as the control group. The patients and controls are all to recept the examinations, including the ordinary MRI, DTI, VEP and OCT. According to the result of the latency of P100 wave, the patients are divided into VEP abnormal eye group ( group 1 ) and VEP normal eye group ( Group 2 ). Then we measure and analysis the mean diffusivity( MD ), the fraction anisotropy( FA ), the latency of P100 wave, the average thickness of retinal nerve fiber layer( RNFL ) of papilla in the four quadrant and the over all 512 test point.  

Results: 1. The FA value declined markedly and MD value increased obviously in patients with prolonged latency of P100 wave. There had significant difference comparing with the controls and patients with normal P100 wave. ( P<0.01 ).  
2. The latency prolonged of P100 wave had significant negative correlation declined FA value of optic nerve, optic tract and and radiation and positive correlation with increased MD value in NMO (P<0.05).  
3. There had significant positive correlation between FA value and Savg,Navg,Iavg,Tavg and Avg of RNFL (P<0.05). And the MD value of optic radiation had significant correlation with Savg,Navg,Iavg,Tavg and Avg of RNFL (P<0.05).  
4. There had significant negative correlation between latency of P100 wave and the Savg,Navg,Iavg,Tavg,Avg of OCT.  

Conclusions: Diffusion tensor imaging could show the small pathological changes in the white matter fibers of visual pathway, and there had the significant correlation between DTI ,VEP and OCT in NMO, suggesting that we can make a more comprehensive assessment to the condition and prognosis through the VEP and OCT in the clinical indicators.
bilateral posterior corona radiata). Then the correlation analyses were conducted between the MTI indicator of magnetization transfer ratio (MTR), and the EDSS score, disease duration, the relapse frequency. The region of interest analyses were performed to obtain that the MTR values of right lentiform nucleus, bilateral globus pallidus and bilateral cingulated gyrus of the NMO group at acute phase were increased when compared with those of the normal healthy control group at stable phase. The MTR values of right caudate nucleus, bilateral globus pallidus, bilateral cingulated gyrus of the NMO group at acute phase were lower than those of the normal healthy control group. The MTR values of bilateral cerebral peduncle of the NMO group at acute phase were lower than those of the normal healthy control group. The MTR values of brain white and gray matter of other regions of interest were not significantly different from those of the normal healthy control group (P > 0.05). The correlation analyses between the MTR values and EDSS score, disease duration, the relapse frequency of the NMO patients at acute and stable phase indicated no significant difference (P > 0.05). The imaging scan of brain gray matter magnetization transfer of NMO patients showed the different MTR values, which suggested that occult injury might exist there. This occult change may be different at acute and stable phases. The occult brain changes of NMO patients may not be related to the EDSS score, disease duration and relapse frequency in the MTI sequence.4

Methods: This is a retrospective study of 40 patients with recurrent ON or simultaneous bilateral ON, who were evaluated at the Samsung Medical Center, Korea, from April 2006 to June 2011. Results: Twenty five patients were AQP4-Ab positive. Seropositive group were predominantly female compared with seronegative group (20/25 vs. 7/15, p = 0.04). The former had a trend to have globally attenuated retinal vessels (6/25 vs. 1/15, p = 0.22) and more attacks of ON (2.96 vs. 2.07, p = 0.18). The 7 patients with initial globally attenuated retinal vessel had worse visual acuity recovery than the remaining 33 (p = 0.02). Retinal nerve fiber layer findings will be presented after finishing the analysis of optical coherence tomography.

Conclusions: Seropositivity of aquaporin-4 antibody may be associated with retinal vasculopathy following ON and subsequent poor recovery of visual acuity.

Poster Session 4

Neurophysiological Study in MS

P-54
EVOKED POTENTIALS IN PATIENTS WITH MULTIPLE SCLEROSIS
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Purpose: Multiple sclerosis is a multi-systemic, recurrent inflammatory disorder that involves central nervous system (CNS). The aim of our study was to investigate the possible neurophysiologic disorder in the central nervous system by means of evoked potentials (EP).

Methods and Results: We studied 35 patients with MS; the mean age was 53.52±11.83 years (yrs) (range 18 yrs to 47 yrs; 17 female and 9 male) and 33 age-matched healthy subjects (control); the mean age was 39.12 ± 13.11 years (19 female and 14 male). All subjects were studied using an electromyogram (EMG) equipment (KEYPOINT, DANTEC, DENMARK). Out of 35 patients, 27 (77.14 %) showed abnormalities of somatosensory evoked potential, 23 (65.71 %) abnormalities of visual evoked potentials.

Conclusion: We conclude that EP measurement which can easily be performed in the electromyography laboratory, are helpful and sensitive method to evaluate neurophysiologic disorders of CNS’ involvement in MS.

Retinal Vascular Changes Following Optic Neuritis In Patients With Neuromyelitis Optica

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Background: Neuromyelitis optica (NMO) have been associated with the disease-specific autoantibody aquaporin-4 (AQP4-Ab), thought to be pathogenic. Previous pathologic series described abnormally thickened vessel walls with narrowing of the lumen in the retrobulbar optic nerves and spinal cords of NMO patients.

Objective: To compare the retinal vascular changes between seronegative and seropositive optic neuritis (ON).
**P-55**

Abnormal Trigeminal Somatosensory Evoked Potential In A Multiple Sclerosis Patient

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**Background:** There are diverse symptoms in multiple sclerosis (MS). Of the symptoms of MS, facial numbness symptoms are vague and easily overlooked. A patient diagnosed as MS was presented with selective involvement of the right trigeminal nerve. The abnormality of the right trigeminal nerve was found in the trigeminal somatosensory evoked potential (TSEP). The presumed diagnosis of MS was subsequently confirmed by MRI showing evidence of demyelinating disease.

**Objective:** We report a case of MS presenting unilateral facial numbness having abnormality of TSEP and emphasized the clinical usefulness of TSEP in the diagnosis of MS.

**Method (case presentation):** A 50 year old man presented with numbness in right cheek area. 1 days later, his facial numbness area is widened to right forehead, around the lip. On neurological examination, right facial hypoesthesia and cerebellar ataxia was detected. On TSEP, the right trigeminal nerve stimulation did not show wave formation. However, left trigeminal nerve stimulation showed normal wave formation and normal latency. Brain MRI revealed T2 high signal intensities in right brachium pontis with T1 focal enhancement suggesting of demyelinating lesion. He was treated on intravenous methylprednisolone 1g for 5 days. His facial numbness and ataxia improved over several days. Unfortunately, because he did not visit the outpatient clinic, follow up brain MRI was not performed.

**Result and conclusion:** There has been a scarcity of references on TSEP. Our study emphasizes its usefulness for the diagnostic workup in patients with MS presenting facial sensory change.

**P-56**

Regional homogeneity of brain default mode network in patients with multiple sclerosis

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**Objective:** To investigate the characteristics of brain default mode network (DMN) of patients with multiple sclerosis (MS) in resting state with functional MRI. To analyze the cognitive function of DMN in MS.

**Method:** 12 relapsing-remitting (RR)MS patients and 13 gender, age, and education matched normal controls experienced resting state fMRI scans.

**Results:** The mean MMSE scores of RRMS patients were 28.33±2.54. The mean MoCA scores of RRMS patients were 24.75±4.12. Compared with normal controls, the RRMS patients showed increased regional homogeneity (ReHo) in Right anterior cingulum gyrus, Left precuneus gyrus, Left superior medial frontal gyrus, Right superior medial frontal gyrus, Left parietal inferior lobe, Right angular gyrus (P<0.05). Compared with normal controls, the RRMS patients showed reduced ReHo in Light temporal lobe (P<0.05).

**Conclusion:** The DMN of RRMS patients was abnormal in resting state.

**P-57**

Cognitive Impairment and Influential Factors in Multiple Sclerosis

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**Background:** Multiple sclerosis (MS) was reported cognitive impairment (CI) that include processing speed, executive function, and working memory.

**Objective:** To study the MS cognitive impairment and their influential factors in China.

**Methods:** This was a cross-sectional study with 36 relapsing-remitting MS (RRMS), 21 secondary progressive MS (SPMS), and 20 healthy controls. Neuropsychological Tests was conducted 8 weeks later including information processing speed, memory, executive functions, language and visual perception. Correlation between CI, depression and fatigue were studied.

**Results:** (1) MS patient groups demonstrated cognitive deficits compared to healthy controls. The Symbol Digit Modalities Test (SDMT), Paced Auditory Serial Addition Task (PASAT) impaired most. SPMS patients were more affected compared to patients with RRMS subtypes, These differences were attenuated after control for physical disability level as measured by the EDSS scores. MS patients were more severely impaired than control group on the verbal learning test, verbal fluency, Stroop C and California card classification test planning time. Language and visual-spatial problems in MS were less common.

(2) Age, depression, EDSS scores and fatigue were related with PASAT and SDMT tests (p<0.05). In the stepwise linear regression analysis, age made a significant contribution to PASAT test, EDSS scores were the first related factor to SDMT test. Depression
and cognitive fatigue had negative influence on auditory verbal learning and verbal fluency test.

**Conclusions:** Problems with processing speed, verbal memory and executive functioning were seen in MS patients, especially SPMS subtype. Age, total lesion load, EDSS scores, depression and fatigue were associated with cognitive impairment.

**P-58**

**Blood flow parameters in the ophthalmic artery in acute and chronic phase of optic neuritis – ultrasound evaluation**

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**Background and objective:** Optic neuritis (ON) is a common manifestation of multiple sclerosis (MS). It occurs due to immune-mediated inflammation of the optic nerve. Some vascular factors that could influence the blood flow in the ophthalmic artery (OA) have been suggested in the pathogenesis of ON as well. The purpose of our study was to evaluate and compare blood flow velocities and resistance (RI) and index in the OA in both orbits in patients with acute and chronic phase of unilateral ON.

**Methods:** Ultrasound measurement of blood flow parameters (PSV, EDV and RI) was performed in 35 consecutive MS patients during acute unilateral ON prior to corticosteroid treatment. The peak-systolic (PSV) and end-diastolic (EDV) velocities and RI were measured in the OA on both sides. We compared results from affected and unaffected orbits using paired t-test. The same measurements were performed in 114 MS patients with the history of acute unilateral ON at least one year before ultrasound exam.

**Results:** We found PSV (p<0.0001) and RI (p<0.0001) in the OA on the side affected with acute ON significantly higher comparing with the unaffected side. In chronic phase of ON we did not observe any significant side difference neither in blood flow velocities nor in the RI (p>0.05).

**Conclusion:** The changes of orbital haemodynamics during acute unilateral ON suggest the role of vasoconstriction of orbital vessels as one of the underlying pathophysiological mechanisms of acute ON. These changes however last shortly and are not observed in the chronic phase of ON.

**P-59**

**RR INTERVAL VARIATION AND THE SYMPATHETIC SKIN RESPONSE IN THE ASSESSMENT OF AUTONOMIC FUNCTION IN MULTIPLE SCLEROSIS.**

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The aim of our study was to evaluate possible autonomic nervous system (ANS) dysfunction in patients with multiple sclerosis (MS), and its correlation with abnormalities of sensorimotor nerve conduction study and clinical autonomic symptoms.

We studied 35 patients with MS, the mean age was 53.5±11.83 years (yrs) (range 18 yrs to 47 yrs; 17 female and 9 male) and 35 age-matched healthy subjects (control); the mean age was 34.19±12.74 years (yrs) (range 24 yrs to 48 yrs; 20 female and 15 male). Mean RR interval and SSR in patients with MS were significantly abnormal than that of the normal subjects (p<0.05).

We conclude that SSR and RR interval variation, both of which can easily be performed in the electromyography laboratory, are helpful and cheap method in combination in the assessment of autonomic function in multiple sclerosis.

**P-60**

**Alterations in circulating levels of vitamin D and the association with clinical characteristics in multiple sclerosis patients**

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**Objective:** To investigate the circulating levels of Vitamin D in multiple sclerosis (MS), and to explore the relationships between vitamin D and the clinical characteristics of MS.

**Methods:** The circulating levels of 25-hydroxyvitamin D$_3$(25(OH) D$_3$) were measured by electrochemiluminescence in 72 MS patients, 24 neuromyelitis optica (NMO) patients and 32 normal controls.

**Results:** (1) Compared to controls, patients with MS or NMO had significantly lower levels of 25(OH) D$_3$ (P<0.01, P<0.05). There was no significant difference between MS patients and NMO patients (P>0.05).
The 25(OH) D$_3$ levels in secondary progressive (SP) MS patients were significantly lower than normal controls ($P < 0.01$), but not significantly different from relapsing-remitting (RR) MS patients ($P > 0.05$). The 25(OH) D$_3$ levels were significantly lower in RRMS patients during exacerbation compared with patients in remission ($P > 0.05$).

**Conclusions:** These data suggest that MS and NMO patients are in a state of vitamin D insufficiency. Both RRMS and SPMS patients show vitamin D insufficiency. Vitamin D insufficiency exacerbated during relapse for RRMS patients.

**P-61**

**The effect of Free Testosterone on Course, Severity, Disease activity and disability in the patients with Multiple Sclerosis**

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**Introduction:** Sex-related difference in the course and severity of Multiple Sclerosis (MS) could be mediated by several sex hormones. This study aimed to investigate the relation between free testosterone concentrations and course, severity, brain damage and disability in Iranian patients with MS.

**Methods:** 37 women with MS and 25 healthy subjects were included in the study as case and control groups. Free testosterone level was assessed by ELISA method. Brain MRI with and without contrast was performed. Expanded Disability status scale (EDSS) and MS subtypes in the patients were collected via a questionnaire.

**Results:** Serum testosterone was significantly lower in women with MS than controls ($P = 0.026$). The free testosterone levels were not associated with EDSS, MS subtype and MRI findings.

**Discussion:** The hormone related modulation of pathological changes does not support the hypothesis that sex hormones play a role in the inflammation, damage and repair mechanism in MS. Although serum levels of these hormones in the patients was significantly lower than controls.

**Background:** Nicotinamide adenine dinucleotide (NAD$^+$) and reduced NAD (NADH) are ubiquitous pyridine nucleotides which are well known to participate in oxidation-reduction reaction during ATP production. These pyridine nucleotides are also involved in various cellular repair mechanisms and may play a crucial role against demyelination and neurodegeneration induced by oxidative stress during chronic inflammation. Indeed, reduced NAD/NADH levels are linked to cell death and may be associated with systemic effects such as fatigue, a common complaint as MS progresses. To our knowledge, no information regarding the role of NAD and NADH has been reported in MS progression.

**Objective:** To investigate NAD$^+$ and NADH levels in serum in patients with different disease stages and forms of MS.

**Methods:** NAD$^+$ and NADH levels were measured in the serum from 209 patients with relapsing-remitting MS (RRMS), 136 with secondary progressive MS (SPMS), 51 with primary progressive MS (PPMS), and 99 healthy controls. All patients were in a clinically stable phase.

**Results:** Serum NAD$^+$ levels were significantly lower in patients with MS compared to controls ($p=0.0012$). Within the MS subgroups NAD$^+$ levels were higher in RRMS ($p=0.001$) compared to PPMS ($p=0.003$) and SPMS ($p=0.005$). Higher levels of NADH ($p=0.002$) and a lower NAD$^+$/NADH ratio ($p=0.009$) were observed in MS patients compared to controls.

**Conclusion:** Serum NAD$^+$ and NADH levels are may be associated with disease progression in MS. Given the importance of NAD$^+$ in energy production it is likely that this is pathogenically important in MS. Indeed, the results point to significant systemic energy depletion.

**P-63**

**Serum Uric Acid Level in Patients with Relapsing-Remitting Multiple Sclerosis**

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Abstract: Uric Acid is a hydrophilic antioxidant product that is said to have a relation with Multiple Sclerosis. The aim of this study was to evaluate the serum level of uric acid in different phases of MS. Serum uric acid was checked in 130 relapsing-remitting MS patients (85 patients in remitting and 45 patients in relapsing phase) and 50 age and sex matched controls using the quantitative enzymatic assay method (ELISA).

The mean level of serum uric acid in remitting and relapsing MS patients were 6.41 (±3.18) mg/dl and 4.76 (±1.66) mg/dl respectively. While compared to the mean level of serum uric acid in the control group [6.33 (±2.94) mg/dl], there was a significant difference between relapsing MS patients and both remitting MS patients (P=0.000) and the controls(P=0.002).

However, the difference between the remitting phase of MS and the control group was not significant (P=0.87). It seems probable that UA plays a sensible role in the prevention of disease activity in MS.

P-64
Comparison of serum levels of copper and zinc among patients newly-diagnosed of Multiple Sclerosis (MS) referred to Kerman Shafa hospital during 2007-2009 by a control group of their relatives
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Introduction: MS is a chronic demyelinating disease of central nervous system. Studies have shown that MS is a result of immune reaction of unknown etiology, but there are several factors known to be effective; such as vitamin D deficiency, smoking, previous infection by Epstein-Barr Virus (EBV), contact to metals and living in high prevalence ecological regions.

Method: This is a case-control study conducted from October 2007 to January 2009. 58 MS patients who were diagnosed by neurologist based on McDonald criteria were selected as the patient group and 39 healthy people from among their relatives who were paralleled with regard to age and sex were selected as the control group and the serum level of copper and zinc was measured and compared in both groups.

Results: There were 48 female and 10 male individuals in patients group and 30 female and 9 male in control group. Both groups were resembled in age and sex. The average serum level of Copper in patients group and the control group were 93.7 – 88.9 micrograms per deciliter respectively and average serum level of Zinc were 36.7 – 40.9 micrograms per deciliter respectively. There was no significant difference between two groups (P =0.459- 0.249 respectively) also no significant difference was seen in different levels of Copper and Zinc among two groups (P =0.551 – 0.377 respectively).

Conclusion: We brought to this theory that if we exclude some disturbing factors that play role in the hemostasis of Copper and Zinc, there will be no difference in serum levels of Copper and Zinc in MS patients comparing to the control group that is similar in genetic and environmental factors.

P-65
Serum Ca and P of patients with multiple sclerosis
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Introduction: Although some studies suggested a link between exposure to trace elements and development of multiple sclerosis (MS), clear information on their role in the etiology of MS is still lacking. This study was conducted to evaluate the relation of serum Ca and P with multiple sclerosis.

Materials and Method: In this cross sectional study the concentrations of Ca and p were determined in the blood of 30 patients with MS and 30 controls. The levels of serum Ca and P were evaluated in both groups and the results were analyzed by paired T-test.

Results: 13 men and 17 women were studied in each of the two groups. When the two groups were compared, an increased level of Ca and a decrement of P in blood of patients were observed (p<0.05).

Conclusions: Increased serum level of Ca may be a risk factor for multiple sclerosis.

P-66
Comparison of Serum lipid profiles between Chinese multiple sclerosis and neuromyelitis optica
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Background: Several studies have demonstrated a significant increase in lipid peroxidation products in brain, plasma and cerebrospinal fluid of MS patients. However, the change of lipid profiles between multiple
Objective: To assess the differences of serum lipid profile in MS, NMO, and normal healthy subjects (NHS) and the associations of serum lipid profile variables with MS and NMO.

Methods: This study enrolled some age and gender patients matched with MS, NMO, and NHS and tested their serum lipids levels: total cholesterol (TC), triglyceride (TG), high and low density lipoproteins (HDL, LDL), apolipoproteinB100 (apoB100), apolipoproteinA-I (apoA-I). The number of episodes, expanded disability status scale (EDSS) on admission, and disease duration in MS and NMO were assessed.

Results: We found higher HDL (P < 0.001), apoA-I (P = 0.007), apoB100 (p = 0.002), and lower LDL levels (P < 0.001) in MS patients, compared to NHS. We also found higher HDL (P < 0.001) and lower LDL levels (P < 0.001) in NMO patients, compared to NHS. Meanwhile, we proved the highest HDL and the lowest LDL levels in MS. EDSS was associated with higher LDL levels (p = 0.028) and Higher apoA-I (p = 0.038) were associated with disease duration in MS. Higher apoA-I levels were associated with EDSS (p = 0.003) in NMO.

Conclusions: Serum lipid profile has different effect in MS, NMO, and NHS. Serum lipid profile could exert a different neurotoxic influence and contribute to discretely demyelination and axonal injury in MS and NMO.

P-67
Serum γ-glutamyl transpeptidase level predicts outcome of patients with neuromyelitis optica
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Background: Many studies have demonstrated that γ-glutamyl transpeptidase (GGT) is a marker of oxidative stress and inflammation, however, little research has been done to examine whether GGT is associated with multiple sclerosis (MS) and neuromyelitis optica (NMO). We performed a retrospective study to explore correlations between GGT level, as well as clinical characteristics of Chinese patients, with MS and NMO.

Patients and Methods: Serum GGT level was measured in 95 MS patients, 111 NMO patients, 87 Parkinson disease (PD) patients and 85 healthy controls. Clinical parameters of MS and NMO patients were also investigated.

Results: NMO patients exhibited significantly greater EDSS scores, as well as higher serum GGT level than MS patients. Compared to healthy controls and PD patients, NMO patients had significantly higher serum GGT level. And in female subgroup, serum GGT level was also significantly higher than that in MS patients and healthy controls. Serum GGT level in NMO patients with MRI active was significantly higher than that in MS patients with MRI active. Serum GGT level in AQP4-seropositive NMO patients was insignificantly greater than AQP4-seronegative NMO patients. A significant correlation existed between serum GGT level, age, and relapse frequency of NMO patients.

Conclusions: Serum GGT level could serve as a NMO marker for differential MS diagnosis, and elevated GGT level might be secondary response to more severe inflammation injury in NMO.

Poster Session 6

Immunological and Immunogenetical Studies in MS and NMO

P-68
Anti-MOG Antibody in Different Types of Immune-mediated Optic Neuritis
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Background: Different types of immune mediated optic neuritis (IM-ON) need different treatment strategy for preventing further neurological impairment, but it is usually difficult to distinct the types only clinically. Aquaporin-4 antibody has low sensitivity in differential diagnosis of IM-ON.

Objective: To investigate the diagnostic value of anti-myelin oligodendrocyte glycoprotein antibody (MOG-Ab) in different types of IM-ON.

Methods: The serum of 129 consecutive cases of immune-mediated optic neuritis (IM-ON group) seen in Neuro-ophthalmology clinic in Department of Neurology, Beijing Tongren Hospital were collected. All IM-ON cases were further classified into four different types as: multiple sclerosis like ON (MS-ON), neuromyelitis optica like ON (NMO-ON), autoimmune...
ON (AON), and other immune mediated ON(O-ON),
MOG-Ab was tested by ELISA. Statistical analysis was
done by SPSS software.

Results: MOG-Ab was positive in 12 of totally 129
included IM-ON patients (9.3%) while in 5 of 20(25%)
MS-ON, none of 13 NMO-ON (0%), 4 of 33(12.1%)
AON, 2 of 63(4.8%) patients. While MS-ON group
showed the highest MOG-Ab positivity, none of 13
NMO-ON cases was positive for MOG-Ab, but this
difference did not reach statistically significant which is
probably due to relatively small numbers.

Conclusions: In different types of immune-mediated
optic neuritis, MS-ON patients showed the highest
MOG-Ab positivity while none of NMO-ON cases was
sero-positive. Even this difference did not reach
statistical significance; MOG-Ab might be helpful to
distinguish NMO-ON from other types of
immune-mediated optic neuritis.

P-69
Myelin oligodendrocyte glycoprotein antibody in
multiple sclerosis and neuromyelitis optica
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Objectives: Whether antibody to myelin
oligodendrocyte glycoprotein (MOG) can be a
diagnostic marker for multiple sclerosis (MS) is still
controversial. One recent study suggested that MOG
index may be a complementary diagnostic marker.
However, this study did not include neuromyelitis
optica (NMO) which might be proven to also have
anti-MOG antibody. Hence, the present study was
undertaken to further investigate MOG index in
patients with MS, NMO and non-inflammatory disease
(NIND).

Methods: 61 MS, 54 NMO and 24 NIND patients were
recruited in this study. Anti-MOG1,125 IgG
concentration in serum and CSF was measured by
ELISA, using the extracellular portion of human MOG
expressed in the human embryonic kidney cells. The
MOG index was calculated based on the anti-MOG1,125
IgG and albumin levels in serum and CSF.

Results: Both MS and NMO had significantly higher
anti-MOG1,125 IgG concentration in serum and CSF
than NIND (P < 0.01) while no statistical differences
existed between MS and NMO. The MOG index was
upgraded in MS (0.82 ± 0.70) compared with NMO
(0.42 ± 0.25, P < 0.01) and NIND (0.32 ± 0.16, P
< 0.01). In diagnosing MS, the sensitivity of MOG
index (51%) was lower than that of oligoclonal bands
(OCB, 85%, P < 0.01). When combination of MOG
index and OCB was applied, the sensitivity increased to
97% with a slight decrease in specificity from 86% to
80%.

Conclusions: While MOG index is inferior to OCB in
diagnosing MS, it may serve as a complementary
diagnostic marker.

P-70
Prevalence Of Serum Anti-Thyroid Antibodies And
Thyroxine In Multiple Sclerosis And Neuromyelitis
Optica
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Background: A high frequency of anti-thyroid
antibodies(ATAbs) has been demonstrated in multiple
sclerosis (MS), but there is a lack of data on the
possible association of serum ATAbs and thyroid
hormones (TH) in MS and neuromyelitis
optica(NMO).

Objective: To determine whether there are differences
in the prevalence of ATAbs and TH in MS and NMO
compared with normal healthy subjects(NHS) and
whether ATAbs correlates with MS and NMO.

Methods: Thirty clinically definite MS, without
interferon-beta treatment, forty NMO patients, and
eighty-eight NHS were included in this study. Serum
ATAbs and TH were measured. The number of
episodes, expanded disability status scale (EDSS) on
admission, and disease duration in patients with MS
and NMO were assessed.

Results: Anti-peroxidase antibodies (TPOAb) were
detected in 4/88 (4.5%) NHS, compared to 7/30
(23.3%) MS (P=0.007) and 17/40 (42.5%) NMO (P<
0.001). Anti-thyroglobulin antibodies (TGAb) were
detected in 5/88 (5.7%) NHS, compared to 5/30
(16.7%) MS (P=0.137) and 11/40 (27.5%) NMO
(P=0.001). TT3 and FT3 were significantly lower in
MS (P=0.001 and P < 0.001, respectively) and NMO
(P=0.006 and P<0.001, respectively ) than that in NHS.
TPOAb titres were significantly higher in NMO than
that in the MS (P=0.004) and NHS (P=0.002). In MS,
The EDSS were associated with TPOAb titres
(rS=0.420, P=0.019) and TGAb titres (rS=0.493,
P=0.006). In NMO, the positive association between
EDSS and TPOAb titres (rS=0.339, P=0.032) were
found.

Conclusions: Our findings demonstrate that serum
ATAbs and TH are different in MS, NMO, and NHS.
NMO has different serum ATAbs from MS patients.
TH may play a different protective role in MS and
NMO. Furthermore, high titres of ATAbs are differently associated with high disability scores in MS and NMO.

P-71 (O-31)
Cerebrospinal fluid levels of IL-21 in multiple sclerosis and neuromyelitis optica
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Background: Multiple sclerosis (MS) and Neuromyelitis optica (NMO) are inflammatory demyelinating diseases of human central nervous system (CNS) with complex pathogenesis. IL-21/IL-21R regulates activation, proliferation, and survival of both T cells and B cells, which are involved in the pathogenesis of MS and NMO. High level of serum IL-21 concentration was observed in NMO. However, levels of CSF IL-21 in MS and NMO patients still remain unknown.

Methods: CSF IL-21 was measured by an enzyme-linked immunosorbent assay (ELISA) in MS (n=20), NMO (n=21) patients and controls (n=16).

Results: CSF concentration of the IL-21 was borderline significantly increased in MS (p=0.115) and noticeably elevated in NMO (p=0.012). In addition, this occurrence was associated with humoral immune activity as shown by high IL-21 levels in autoantibody-positive subgroup (p=0.027) and correlation between IL-21 and complement in NMO cohort (p=0.023).

Conclusions: The concentration of CSF IL-21 was noticeably elevated and might have a positive correlation with humoral immune activity in NMO.

P-72
Plasma levels of IL-17 and IL-23 in the patients with Multiple Sclerosis
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Introduction: Multiple sclerosis (MS) is the most common demyelinating disease of central nervous system. Recently a subset of T-helper lymphocytes named TH17 are known to be involved in the induction and progression of EAE (Experimental autoimmune encephalomyelitis). These cells produce IL-17 under stimulation of IL-23 secreted by antigen presenting cells that both of them are pro inflammatory cytokines. The aim of this study was to measured plasma level of IL-17 and IL-23 and investigating association of their plasma concentrations with sex, age at disease onset, the disease severity, disease subtype and MRI enhancement of Iranian patients suffering MS.

Patients and Methods: A total of 41 patients with MS were enrolled in the study, and were compared with 41 age and sex matched control subjects. IL-17 and IL-23 in plasma samples were determined by enzyme linked immunosorbent assay method. (ELISA)

Results: MS patients had approximately similar plasma levels of IL-17 and IL-23 compared to the controls. Male patients had significantly higher levels of IL-23 compared to their healthy controls. (P value: 0.047)

Discussion: increased plasma levels of IL-23 in male patients comparing to controls may be suggestive of role of IL-23 in differentiation and function of TH17 cells which enhances IL-17 production in the MS patients.

P-73
Interferon-beta reduces peripheral blood IFN-γ and IL-17-producing T cells in patients with multiple sclerosis
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Background: IFN-γ-producing T helper (Th) 1 cells and IL-17-producing Th17 cells are thought to be crucial for development of multiple sclerosis (MS). It is recently reported that newly discovered IL-9-producing Th9 cells exert both aggravating and suppressive roles on experimental autoimmune encephalomyelitis (EAE), an animal model of MS. Interferon-β (IFNβ) is now widely used as one of disease modifying drugs for MS, but effects of IFNβ on Th9 and Th17 cells in MS patients are still controversial.

Objective: To clarify effects of IFNβ on various T cell subsets in peripheral blood of MS patients.

Method: We analyzed proportions of CXCR3 (Th1), CCR6 (Th17), CCR4 (Th2), CCR3 (Eosinophil)-positive cells and IFN-γ-producing CD4+ and CD8+ T cells in peripheral blood by flow cytometry in 34 MS patients (10 IFNβ-treated and 24 untreated) and 15 healthy controls (HCs).
Result: IFNβ-treated MS patients showed significantly lower percentages of IFN-γ+CD4+T cells and IL-17+CD8+T cells than untreated MS patients. Percentages of CCR6+CD4+T cells, IFN-γ+CD4+T cells, IL-17+CD4+T cells and IFN-γ+CD8+T cells in IFNβ-treated patients were significantly lower than in HCs. There were no significant differences in CXCR3, CCR4, CCR3, IL-9 and IL-4-positive cells among the three groups.

Conclusions: IFNβ appears to exert its therapeutic effect partly through reducing IFN-γ-producing CD4+T cell and IL-17-producing CD8+T cells in peripheral blood of MS patients.

P-74
Circulating CD4+CXCR5+T cells were increased in patients with Neuromyelitis optica and positively associated with Th17 cells
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Background: Circulating Th17 cells and serum IL-17 are significantly increased in patients with neuromyelitis optica (NMO) and multiple sclerosis (MS), particularly during relapses. While the discovery of aquaporin-4 autoantibody (AQP4-Ab) suggested that NMO was mediated by humoral immunity. However, the relationship between Th17 and antibody secretion is still unclear. CD4+CXCR5+T follicular helper (Tfh) cells are a recently described novel subset of CD4+T helper lymphocytes that play an important role in T-B cell cooperation.

Objectives: Evaluated circulating CD4+CXCR5+Tfh cells and Th17 cell count in peripheral blood samples of patients with NMO during relapse. Correlation analysis of CD4+CXCR5+Tfh cells, Th17 cells and Expanded Disability Status Scale (EDSS) score.

Methods: Twenty-two NMO, 31 MS, and 14 healthy controls were recruited. CD4+CXCR5+Tfh cells and Th17 cells were counted using flow cytometry, and serum levels of interleukin (IL)-6 and IL-21 were measured by ELISA.

Results: Circulating CD4+CXCR5+Tfh cells were elevated in the NMO group compared with the other groups. CD4+CXCR5+Tfh were also markedly higher in the MS group than the control group. There was also a positive correlation between CD4+CXCR5+Tfh cells with both EDSS scores and Th17 cell counts in NMO patients.

Conclusions: Tfh cells may play an important role in the pathological mechanism of NMO.

P-75
Serum level of interleukin-6 in Chinese patients with multiple sclerosis
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Background: Interleukin-6 (IL-6) is a pleiotropic pro-inflammatory cytokine. There are inconsistent conclusions about the expression of IL-6 in multiple sclerosis (MS) patients.

Objective: To investigate the serum concentration of IL-6 in patients with relapsing-remitting MS (RR-MS), compare the difference between males and females, and explore the correlation between the serum concentration of IL-6 and clinical parameters.

Methods: We compared the serum concentration of the pro-inflammatory cytokine IL-6 in 39 patients with MS and 39 healthy controls matched with sex and age. The serum IL-6 concentration was measured by FlowCytomix, a kind of cytometric bead-based assay. Correlations between the serum level of IL-6 and disability (expanded disability status scale, EDSS), disease duration and the number of relapse were examined.

Results: The frequency of subjects with detectable level of IL-6 was significantly higher (p = 0.005) in MS patients than healthy controls, and the serum concentration of IL-6 was observed significantly higher (p = 0.004) in MS patients than healthy controls. When data were analyzed by gender, statistical significances between MS patients and healthy controls were observed only in females, although the frequency with detectable level and the serum concentration of IL-6 were higher in male MS patients than male controls. The number of relapse was found significantly positively (p = 0.009) correlated with the serum level of IL-6 in female MS patients.

Conclusions: IL-6 is involved in the pathogenesis of
The number of relapse is positively correlated with the serum IL-6 concentration in female MS patients, which may suggest that IL-6 serum level can be used as an indicator of the course development in female MS patients.

**P-76**

**Deficiency of natural killer cells in patients with multiple sclerosis is associated with aberrance of interleukin-7**

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**Purpose:** An aberrance of the immune system to discriminate self from non-self is believed to contribute to the emergence of autoimmune diseases such as multiple sclerosis (MS), a condition derived from the immune-mediated damage to myelin and other components of the brain and spinal cord. Natural killer (NK) cells are significant players in the immune system; expansions of NK cells via engagement of common γ-chain cytokine IL-2 receptor reduce disease activities of MS and in the animal model experimental autoimmune encephalomyelitis. These observations prompted us to explore the immune phenotypes and functions of NK cells in MS. Methods: We measured of circulating NK cell growth factors in patients with MS; characterized expression of IL-7 receptors on NK cells by flowcytometry and measured NK cell proliferation in recipient mice. Results: we demonstrated that the numbers of NK cells are reduced and their cytolytic activities are compromised in patients with MS. This deficient phenotype of NK cells is not due to their intrinsic features, because these cells isolated from patients with MS can proliferate equally well as NK cells from normal subjects in NK cell deficient mice upon cell transfer. Furthermore, we found that NK cells express the IL-7 receptor CD127 and a reduction of NK cells appears to correlate with a low level of IL-7 and in patients with MS, whereas other NK cell growth factors IL-2, IL-15 and IL-21 were elevated. Conclusion: this study reveals the aberrance of NK cell in MS and its potential underlying mechanisms and further establishes that NK cells serve as an important disease player as well as a therapeutic target in MS and other autoimmune disorders.

**P-77**

**IL-22 secreting CD4+ T cells in the patients with neuromyelitis optica and multiple sclerosis during relapse**

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**Background:** IL-22 secreting CD4+ T (Th22) cells and interleukin (IL)-22 are involved in the pathogenesis of many autoimmune diseases. The functional role of Th22 cells in neuromyelitis optica (NMO) and multiple sclerosis (MS) were rarely reported.

**Objective:** To measure the proportion of Th22 cells, Th17 cells, CD4+IL-22+IL-17A+ T cells and serum concentrations of IL-22 in patients with NMO and MS comparing with healthy controls (CTLs). To further investigate whether Th22 cells are involved in the pathogenesis of NMO and MS.

**Methods:** Flow cytometry were used to assess T cells subsets in peripheral blood mononuclear cells (PBMCs) from 21 patients with NMO, 15 with MS and 12 CTLs. serum IL-22 concentrations from each group were measured by ELISA.

**Results:** The proportion of Th22 cells in NMO and MS were higher than CTLs(1.37±0.87% VS. 0.55±0.51%, P<0.01; 1.13±0.72% VS. 0.55±0.51%, P<0.01). Serum IL-22 levels were also increased in NMO and MS. A positive correlation between the proportion of Th22 cells and Th17 cells was only found in patients with NMO (r=0.458, P=0.037) but not in MS. In addition, we have not found that Th22 cells have correlation with serum IL-22 concentration in patients with NMO or MS.

**Conclusions:** The proportion of Th22 cells, Th17 cells and serum IL-22 were increased in patients of NMO and MS. Our findings suggest that increased Th22 cells and serum IL-22 may play an important role in patients with NMO and MS, similar to Th17 cells.

**P-78**

**Dysregulation of Surface Marker Expressions on Peripheral Blood Monocytes in Multiple Sclerosis**

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Background: In multiple sclerosis (MS), monocytes play a pivotal role in the disease progression. Human peripheral blood monocytes are consisted of three different subtypes; CD14+CD16 (classical type), CD14+CD16+ (non-classical type) and CD14+CD16- (intermediate type). These subtypes are known to have different functions, but little is known about the precise roles in MS.

Objective: To clarify dysregulation of surface marker expressions on monocyte in MS patients, according to anti-aquaporin-4 (AQP4) antibody status and treatments with predonisolone (PSL).

Method: Blood samples were collected from 54 MS patients (including 19 anti-AQP4 antibody-positive (AQP4+) or 35 anti-AQP4 antibody-negative (AQP4-) patients) and 42 healthy controls. The surface expressions of CCR2, CX3CR1, CD64 and CD62L were analyzed in the three subtypes of monocyte subpopulations by flow cytometry.

Result: In MS patients, CCR2 expressions on classical type monocytes were down-regulated (CCR2 positivity rate, healthy controls vs. MS = 80.01 ± 11.78% vs. 62.29 ± 19.68%, p < 0.0001). Intriguingly, the CD64 expressions on all types of monocytes were up-regulated on AQP4+ patients compared to AQP4- patients. In addition, the CD64 expressions were down-regulated after the treatment with PSL in AQP4+ patients.

Conclusion: Our data suggest abnormalities of monocytes’ characteristics during disease progression and by treatments in MS and NMO patients. Down-regulation of CCR2 and up-regulation of CD64 both indicate differentiation of monocytes into macrophages, implicating active roles of monocytes in disease progressions in MS and NMO, and modification of monocyte function may become a new target for MS treatment.

P-79
Notable Increased Cerebrospinal Fluid Levels of Soluble Interleukin-6 Receptor in Neuromyelitis Optica
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Background: Interleukin-6 (IL-6) is proinflammatory cytokine involved in maintenance of humoral response in various autoimmune disorders, including multiple sclerosis (MS). Binding to IL-6, soluble form of IL-6 receptor (sIL-6R) can activate biological responses in cells. Concentration of IL-6 in cerebrospinal fluid (CSF) is elevated in patients with Neuromyelitis optica (NMO). However, whether levels of CSF sIL-6R are elevated in NMO patients still remain unknown.

Objective: To measure the CSF concentration of IL-6 and sIL-6R in NMO and MS patients, and to investigate the possibility of IL-6/sIL-6R to use as sensitive biomarkers for diseases activity.

Methods: CSF concentrations of IL-6 and sIL-6R were measured by enzyme-linked immunosorbent assay (ELISA) in NMO (n=22), MS (n=18) patients and controls (n=14).

Results: The concentration of IL-6 was higher in NMO cohort than MS (p=0.032) and the controls (p=0.023). And NMO subgroup also had higher levels of sIL-6R (NMO vs MS, p=0.002; NMO vs controls, p<0.001). CSF sIL-6R was associated with Expanded Disability Status Scale (EDSS) score in NMO (p=0.005), but not in MS patients (p=0.891). In MS subgroup, a correlation between sIL-6R concentration and CSF WBC was observed (p=0.034).

Conclusions: Our study revealed that the CSF sIL-6R was increased, and correlated with diseases activity in NMO patients.

P-80
The serum and cerebrospinal fluid levels of CXCL13 in clinical isolated syndrome, multiple sclerosis and neuromyelitis optica and their correlation study
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Objective: To investigate the correlations between B lymphocyte chemoattractant - 1 (BLC - 1/CXCL13) level in serum and cerebrospinal fluid (CSF) and disease progress, extended disability status scale (EDSS) score and MRI scanning in patients with clinical isolated syndrome (CIS), relapsing-remitting multiple sclerosis (RRMS), and neuromyelitis optica (NMO).

Methods: 18 cases of CIS, 22 cases of RRMS, 21 cases of NMO, and 17 cases of neurological non-inflammatory disease (NND) (as a control group) were collected. The CXCL13 level in serum and CSF was detected by ELISA test method, and compared
Conclusions: In NMO patients, CSF BAFF and APRIL may be key factors of B cell immune response and reflect disease activity in acute relapse of NMO and MS. BAFF/APRIL increased in NMO patients was still unclear.

Objective: To measure the CSF BAFF and APRIL concentration of in NMO patients, and explore their relationship with disease activity in NMO.

Methods: CSF BAFF and APRIL was measured by an enzyme-linked immunosorbent assay (ELISA) in NMO (n=22), MS (n=18) patients and controls (n=14).

Results: Concentration of BAFF and APRIL in NMO patients were significantly higher than MS and controls. CSF BAFF and APRIL levels in MS patients were also higher than controls. CSF BAFF levels were positively correlated with Expanded Disability Status Scale (EDSS) scores in NMO and MS patients. CSF APRIL levels were also associated with EDSS scores in NMO, but not in MS.

Conclusions: BAFF/APRIL system may regular B cells and T cell activation in acute relapse of NMO and MS. In NMO patients, CSF BAFF and APRIL may be key factors of B cell immune response and reflect disease severity.

P-82

Study of correlation between MBP, MBPA and OCB of multiple sclerosis patients

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Objectives: To analyze the relationship between oligoclonal band(OCB) and the level of the Myelin basic protein(MBP) and myelin basic protein antibodies(MBPA) in the cerebrospinal fluid(CSF) and serum.

Materials and methods: 40 paired CSF and serum samples were obtained from 40 cases of MS patients, OCBs were detected using isoelectric focusing and avidin biotin-peroxidase complex technique. MBP and MBPA were detected respectively by double antibody sandwich ELISA and indirect ELISA.

Results: The concentration of MBP, MBPA in CSF was higher respectively than that in serum, the concentration of MBP, MBPA in CSF had positive linear correlation with that in serum. The concentration of MBP, MBPA in CSF and serum in OCB positive patients were higher than that in OCB negative patients. The concentration of MBP, MBPA in CSF and serum in patients who were in acute episode course were higher than that in patients who were in remitting course.

Conclusions: MS appears to have demyeliantion mediated by immunity, also have change of the BBB.

P-81

Cerebrospinal fluid BAFF and APRIL levels in neuromyelitis optica and multiple sclerosis patients during relapse

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Background: BAFF (B-cell activating factor of the tumor necrosis factor family) and APRIL (a proliferation-inducing ligand) are two of the fundamental survival factor for B cells. Many studies have shown that BAFF levels were elevated in MS patients. However, whether the levels of CSF BAFF/APRIL increased in NMO patients was still unclear.

Objective: To measure the CSF BAFF and APRIL concentration of in NMO patients, and explore their relationship with disease activity in NMO.

Methods: CSF BAFF and APRIL was measured by an enzyme-linked immunosorbent assay (ELISA) in NMO (n=22), MS (n=18) patients and controls (n=14).

Results: Concentration of BAFF and APRIL in NMO patients were significantly higher than MS and controls. CSF BAFF and APRIL levels in MS patients were also higher than controls. CSF BAFF levels were positively correlated with Expanded Disability Status Scale (EDSS) scores in NMO and MS patients. CSF APRIL levels were also associated with EDSS scores in NMO, but not in MS.

Conclusions: BAFF/APRIL system may regular B cells and T cell activation in acute relapse of NMO and MS. In NMO patients, CSF BAFF and APRIL may be key factors of B cell immune response and reflect disease severity.

P-82

Study of correlation between MBP, MBPA and OCB of multiple sclerosis patients

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Objectives: To analyze the relationship between oligoclonal band(OCB) and the level of the Myelin basic protein(MBP) and myelin basic protein antibodies(MBPA) in the cerebrospinal fluid(CSF) and serum.

Materials and methods: 40 paired CSF and serum samples were obtained from 40 cases of MS patients, OCBs were detected using isoelectric focusing and avidin biotin-peroxidase complex technique. MBP and MBPA were detected respectively by double antibody sandwich ELISA and indirect ELISA.

Results: The concentration of MBP, MBPA in CSF was higher respectively than that in serum, the concentration of MBP, MBPA in CSF had positive linear correlation with that in serum. The concentration of MBP, MBPA in CSF and serum in OCB positive patients were higher than that in OCB negative patients. The concentration of MBP, MBPA in CSF and serum in patients who were in acute episode course were higher than that in patients who were in remitting course.

Conclusions: MS appears to have demyeliantion mediated by immunity, also have change of the BBB.
permeability and the release of the MBP. MBP may be a kind of antigen producing the OCB, and MBPA may be the composition of the OCB. MS has obvious demyelination, MBP in CSF and serum can be considered as the indicator of the disease activity.

P-83
Oligoclonal Bands in Chinese patients with demyelinating diseases of the central nervous system
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**Objectives:** To evaluate the clinical significance of oligoclonal bands (OCBs) for the diagnosis of demyelinating diseases of the central nervous system in China.

**Methods:** We analyzed retrospectively clinical data and cerebrospinal fluid oligoclonal bands of 270 patients of central nervous system demyelinating diseases, including 116 cases of multiple sclerosis (MS) patients, 80 cases of neuromyelitis optica (NMO) patients, 21 cases of acute disseminated encephalomyelitis (ADEM) patients, 40 cases of myelitis patients and 13 cases of patients with optic neuritis. OCBs were detected in 270 patients using isoelectric focusing and avidin biotin-peroxidase complex technique. The results were compared among the 5 groups.

**Results:** OCB positive rate was 30.17% in MS group, 20.00% in NMO group, 4.76% in ADEM group, 12.50% in myelitis group, and 15.38% in optic neuritis group. OCB positive rate in MS group was higher than that in other groups (P < 0.01); OCB positive rate in NMO group was higher than that in myelitis and optic neuritis group (P < 0.01), there was no significant difference in the frequencies of positive OCBs between myelitis group and optic neuritis group, that in ADEM group was lowest (P < 0.01).

**Conclusions:** In the central nervous system demyelinating disease, the detection of OCBs was of differential diagnostic value in the diagnosis of the five groups, but MS patients with OCB positive rate was lower than that reported in Western countries. It is necessary to find more sensitive cerebral spinal fluid indicators for diagnosis.

P-84
Diagnostic efficacy of the flow cytometric aquaporin-4 autoantibody assay: comparison with conventional cell based assay.

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**Background:** Though detection of AQP4 antibodycan be essential in the diagnosis of patients with NMO, its sensitivity varies greatly according to the method of assay.

**Objective:** To establish a highly sensitive and specific anti-AQP4 antibody using flow cytometry and to compare it with that of the conventional cell-based assay (CBA).

**Methods:** Human embryonic kidney-293 cell was transfected with human aquaporin-4 (M23) cDNA. Serum samples from clinically definite NMO (n=20), high risk for NMO group (n=49), classic MS (n=12), other idiopathic inflammatory demyelinating disease (n=35), and negative controls (n=24) were tested with both flow cytometry (SNUH) and conventional CBA (Weatherall Institute of Molecular Medicine).

**Results:** ROC curve for the results of the flow cytometric assay and the conventional CBA showed the areas under the curve (AUCs) of 0.953. The sensitivity of flow cytometry and conventional CBA were 96% and 91% respectively in definite NMO group, 21.7% and 25.0% in high risk for NMO group, 5.3% and 7.9% in other IIDDs group. Both assays showed no positive results in classic MS group and in negative controls. The kappa coefficient for these two tests was very high and was 0.761.

**Conclusion:** Both the flow cytometry and conventional CBA are highly specific and also sensitive in identifying patients with AQP4-Ab, and these two assay methods showed a very good agreement. However, because a small number of patients (3.6%), showed disagreement of results, we suggest that complementary adaptation of those two highly sensitive antibody assays can produce the most accurate outcomes.
**P-85**
The Removal Method of Myelin Basic Protein Antibody in CSF from Patients with Multiple Sclerosis
Qin Xuemin

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**Background:** Myelin basic protein antibody (MBP-Ab) is commonly seen in CSF of patients with multiple sclerosis (MS). It has been reported that CSF filtration can alleviate the MS symptoms.

**Objective:** To setup an adsorbent for removing MBP-Ab from CSF in MS patients and to assess its absorption efficacy.

**Methods:** CSF samples were from 26 cases with MS and 11 cases with non-MS. MBP-Ab concentration was determined by ELISA. The adsorbent was constructed by coating biotin-MBP68-86 to Dynabeads® M-280 Streptavidin. The adsorption rate was calculated by formula (MBP-Ab before absorption –MBP-Ab after absorption) / MBP-Ab before absorption. Various factors such as temperature, shaking, buffer and incubation time were assessed.

**Results:** The adsorption rates under shaking for 60mins in 37℃ were higher than those staying overnight in 4℃ (95.76%±1.47%; 81.95%±1.74%, P < 0.01). The adsorption rates with or without shaking were statistically different (95.54%±1.74%; 82.65%±3.00%, P < 0.01). The adsorption rates between PBS plus buffer and PBS were not different (94.52%±2.15%; 93.53%±2.01%, P=0.427). The adsorption rates of MS samples were higher than that of non-MS samples (94.59%±1.35%, 6.68%±1.31%, P < 0.01). With the increase of incubation time, the adsorption rates were increased from 60.81%±5.02% to 95.45%±1.39%.

**Conclusion:** The method established in this study can effectively remove MBP-Ab from CSF in MS patients in vitro. The higher adsorption rates could be achieved in 37℃, shaking, prolonging the incubation time.

**P-86 (O-29)**
Relationship Between Human Leukocyte Antigen Polymorphisms and Disease Susceptibility in Japanese Patients with Multiple Sclerosis, Neuromyelitits Optica, or Atopic Myelitis
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**Background:** The association between human leukocyte antigen (HLA) polymorphisms and disease susceptibility or resistance in Japanese patients with multiple sclerosis (MS) or neuromyelitis optica (NMO) has been reported. However, the HLA polymorphisms of patients with atopic myelitis (AM), which selectively involves the spinal cord, have never been studied.

**Objective:** This study aimed to clarify the differences in the pattern of polymorphisms of HLA-DRB1 and -DPB1 alleles among patients with MS, NMO, and AM.

**Methods:** Phenotype frequencies of HLA-DRB1 and -DPB1 alleles of 55 patients with AM, 145 patients with MS, and 116 patients with NMO were compared with those of 367 unrelated healthy controls in Japan.

**Results:** Compared with the controls, the DPB1*0201 allele was significantly more frequent in patients with AM (54.5% vs. 31.9%, corrected P value (Pc) = 0.0150, odds ratio (OR) = 2.564). Among patients with MS, individuals with the DPB1*0301 or DRB1*0405 allele had a significantly higher risk for MS (OR = 3.715 and 2.230, respectively), whereas among patients with NMO, individuals with the DPB1*0501 or DRB1*1602 allele had a significantly higher risk for NMO (OR = 2.394 and 8.988, respectively). In contrast, patients with MS and NMO shared the DRB1*0901 allele as a protective allele (OR = 0.281 and 0.169, respectively).

**Conclusions:** Distinct HLA polymorphisms exist among MS, NMO, and AM in Japan, especially on the HLA-DRB1 and -DPB1 alleles. The DPB1*0201 allele is specifically associated with susceptibility to AM, whereas the DRB1*0901 allele, strongly protective for MS and NMO, shows no resistance to AM.

**P-87**
Association of susceptibility to multiple sclerosis in Southern Han Chinese with HLA-DRB1, -DPB1, -DQB1 alleles and DRB1-DPB1 haplotypes: distinct from other populations
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**Background:** Association of HLA class II with multiple sclerosis (MS) has been not well documented in Chinese.

**Objective:** To examine the association of HLA class II with multiple sclerosis (MS) of Southern Han Chinese populations, and to investigate the Association of susceptibility to multiple sclerosis in Southern Han
Chinese with HLA-DRB1, -DPB1, -DQB1 alleles and DRB1-DBP1 haplotypes.

**Methods:** In the two different period studies, we examined genotyping of HLA-DRB1 and -DPB1 alleles and DRB1-DBP1 haplotypes of 60 patients with conventional MS and 95 controls in the former study, and of HLA-DQB1 alleles of the 42 patients with conventional MS and 48 controls in the latter study.

**Results:** In the former study, we found that frequency of the DPB1*0501 allele was significantly higher in patients (90%) than in controls (67.4%) (p = 0.0013, p corr = 0.025). DRB1-DBP1 linkage haplotype in patients (8.33%) was significantly higher than in controls (0%) (p < 0.0001) and the carriage rate of this haplotype was significantly increased in patients (15%) as compared with controls (0%) (p = 0.00013, p corr = 0.003). In the latter study, the frequency of the DQB1*0502 allele was significantly higher in patients (35.7%) than in the controls (8.9%) (p = 0.0018, p corr = 0.027).

**Conclusions:** We found both the HLA-DBP1*0501, DQB1* 0502 allele and the DRB1*1602- DPB1*0501 haplotype are strong predisposing factors for conventional MS in this population.

**P-88**

**HLA-DRB1/DPB1 Haplotypes in Multiple sclerosis and Neuromyelitis optica Patients**

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**Background:** Multiple sclerosis (MS) and Neuromyelitis Optica (NMO) are both chronic neuro-inflammatory diseases believed to arise from complex interactions of environmental and genetic factors. HLA-DRB1*1501-DQA1*0102-DBP1*0602 haplotype was the strongest associated haplotype of MS in Caucasian populations. However, similar researches in NMO were rare, especially in Chinese patients.

**Objectives:** To investigate the association of haplotypes of HLA-DRB1/DPB1 genes with MS and NMO patients in China.

**Methods:** Fifty-five MS patients, 30 NMO patients and 93 healthy controls (CTLs) were enrolled. The HLA-DRB1/DPB1 alleles of the subjects were determined by sequencing-based typing. The haplotypes were analysed by software haplovie 4.2. Pearson Chi-square test were performed to compare the haplotypes frequencies among groups.

**Results:** The frequency of DRB1*1602-DBP1*0501 haplotype was significant lower in MS patients than in NMO patients ($P_{corr}<0.001, P_{corr}=0.040, OR=0.045, 95\% CI:0.005-0.377$). This haplotype was also lower in MS patients than in CTLs ($P_{corr}=0.006$), but there was no statistical significance after Bonferroni-Dunn correction ($P_{corr}=1.000$).

**Conclusions:** The frequency of DRB1*1602-DBP1*0501 haplotype was significant lower in MS patients than in NMO patients.

**Poster Session 7**

**Treatment for MS**

**P-89**

**Therapeutic efficacy of plasma exchange in acute attacks of multiple sclerosis.**

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**Background:** Plasma exchange (PE) is applied to treat severe acute episodes of multiple sclerosis (MS) unresponsive to corticosteroids.

**Methods:** We retrospectively reviewed the medical records of 13 patients unresponsive to corticosteroids consecutively treated by PE between January 2010 and January 2012. The EDSS scores after PE were measured to analyze the primary outcome.

**Results:** 10 patients (76.9%) were women, and the median age was 38 years (range 23–66 years). All patients had multiple sclerosis. At PE onset, the median EDSS score was 6.0 (range 2.5–8.5). Six patients (46.2%) improved EDSS score < 2. Five patients (38.5%) improved EDSS score (2–4). Two patients (15.4%) improved EDSS score (>4). Among the all cases treated with PE, the EDSS scores after treatment (3.846± 0.65) were statistically significantly decreased, as compared with the scores before treatment (6.154± 0.61). ($P*<0.001$)

**Conclusions:** EDSS score was significantly decreased in all 13 patients after PE treatment. The average EDSS score was decreased in 2 points. This study further supports the efficacy of plasma exchange in the treatment of steroid unresponsive severe acute episodes of MS.

**P-90**

**Observation of Multiple Sclerosis Relapses with Different Glucocorticoid Pulse Treatment**

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Background: There is a variety of treatment strategies for Multiple sclerosis (MS), glucocorticoid treatment, however, is recommended as the first-line treatment of MS relapses in many countries guidelines. It was no evidence that the risk of subsequent relapses would be influenced by long-term use of glucocorticoid treatment.

Objective: Observe the Relapsing Remitting Multiple Sclerosis (RRMS) patient in the acute phase after different methods of methylprednisolone (MP) pulse therapy, including annual relapse rate, side effects, hospital stay and hospital costs.

Methods: 42 case of RRMS patients staying at the Jiangxi Provincial People's Hospital in acute phase were collected from 2005 to 2010, among which, 15 cases of IV methylprednisolone without a tapering dose (1.0g × 5d, short-term group), 27 case were tapered slowly over 28 days (IV MP 1g/0.5g/250mg/120mg/60mgx3d, followed by oral 32mg/16mg/8mgx3d, 4mgx4d, Decreasing group).

Results: MP for relapsing forms of RRMS is safe and effective. Two groups are no significant difference in the relapse rate and side effects. Nevertheless, relating to the hospital stay and hospital costs, short-term group significantly less than decreasing group.

Conclusions: At present, the double-blind, randomized, controlled trials and comparing MP treatment of MS are scarce and evidence-based medicine is limited. Glucocorticoid administration, dosage and withdrawal methods still remain controversial. This article only to simple retrospective analysis glucocorticoid pulse therapy of two kinds of withdrawal, thus the conclusion has certain limitations. For more evidence-based medicine and a more rational clinical medication, glucocorticoid treatment of RRMS deserves more clinical studies.
Background: Long-term observations are critical to understand the chronic disease course of patients with MS.

Objective: The BENEFIT Extension study evaluated the impact of early treatment with interferon beta-1b (IFNB-1b) in patients with a first event suggestive of MS over an 8-year study period.

Methods: In the placebo-controlled phase, patients were randomised to IFNB-1b 250 μg sc, eod or placebo for 2 years or until clinically definite MS (CDMS). Patients were then eligible for an open-label follow-up study with IFNB-1b, but were allowed to take other, or no medication. Thereafter, an observational extension study enrolled patients randomised and treated at least once in the placebo-controlled phase.

Results: 284 (IFNB-1b: 176, placebo: 106) of the original 468 BENEFIT patients were enrolled in the extension and followed for a maximum of 8.7 years. Across the entire analysis period (N=468), early treatment reduced risk of developing CDMS by 32.2% (hazard ratio 0.678, \( p=0.0029 \)) and also annualized relapse rate (risk ratio 0.771, \( p=0.0012 \)). On average, patients remained stable over time, with a median EDSS of 1.5. Of the patients originally randomised and treated, 444 (94.9%) received any DMT (including study medication) at any time during the study period, 363 (77.6%) exclusively received IFNB-1b, while only 31 (6.6%) received other DMTs that may be considered escalation therapies.

Conclusions: These data support early initiation of IFNB-1b in patients with a first event suggestive of MS. After 8 years, there was still a risk reduction of CDMS and relapse risk reduction in favor of early treatment.

P-93

MS-Related Causes of Death and Clinical Outcomes in Patients from the 21-Year Long-Term Follow-up Study of Interferon Beta-1b


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Background: Because randomised clinical trials (RCTs) typically focus on short-term outcomes, long-term data on the effects of disease-modifying therapies for patients with MS are critically important.

Objective: To evaluate the effect of interferon beta-1b (IFNB-1b; Betaseron®) on long-term clinical outcomes and examine underlying causes of death.

Methods: The 21-Year Long-Term Follow-up study was a multicentre, observational study evaluating effects of IFNB-1b on clinical outcomes 21 years after randomised treatment. All patients enrolled in the pivotal RCT were eligible. Patients had been randomized to receive IFNB-1b 50 μg (n=125), IFNB-1b 250 μg (n=124), or placebo (n=123) every other day for a median of 3.8 years up to 5 years. An Adjudication Committee determined causes of death using an algorithm to identify MS-related deaths.

Results: After a median of 21.1 years from enrollment, 98.4% of subjects from the study were identified, including 81 deaths. Patients originally randomized to IFNB-1b 250 μg showed significant reductions in all-cause mortality (46.8%) compared with placebo (log-rank, \( p=0.0173 \), hazard ratio 0.532). Cause of death information or its relationship to MS was available for 85% of cases. 78.3% of adjudicated deaths were determined to be MS related, including 67.5% in the placebo group. Pulmonary infections were particularly common in this group. 28.3% of patients were disabled and 60% of subjects had ceased work due to MS.

Conclusions: Greater mortality was observed in subjects initially randomised to placebo than active treatment, mostly due to MS-related causes. Thus, IFNB-1b therapy may reduce mortality by decreasing MS-related deaths.

P-94 (O-35)

B-cell controlled therapy with rituximab

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Background: Rituximab, a monoclonal antibody, selectively depleting CD20+ B cells, has demonstrated efficacy in reducing disease activity in relapsing remitting MS, in subgroups of primary progressive multiple sclerosis (PPMS) and Neuromyelitis optica (NMO). Case studies suggest that the recurrence of
B-lymphocytes can be correlated with the reactivation of inflammatory activity.

**Purpose:** To evaluate a standardized treatment protocol (375mg/m2 iv) given once at the individual time B-cell return.

**Methods:** 15 patients (11 SPMS, 1 PPMS, 3 NMO) who failed first line therapy received 375 mg/m2 rituximab iv.. Blood samples were taken before, after 4 months, then every two months following treatment. Patients received the next treatment course as soon as the B lymphocytes increased. The primary endpoints were confirmed disease progression (CDP) by an increase in EDSS and results of MRI scans by paraclinical progression and presence of gadolinium-enhancing lesions. Secondary endpoints: the annualized relapse rate and safety parameters.

**Results:** 11 patients received three doses of rituximab, the remaining four patients two, four, five and six courses. Time between the courses varied according to the individual B-cell count between month four and twelve. Expanded disability status scale (EDSS) was registered before the first course and every following, ranging from 2.5 to 8.0. Patients showed a decreased mean annualized relapse rate (from 1.67 to 0.73) with one patient improving from 12 relapses to one per year, and stabilization in mean EDSS score (from 5.6 to 5.66). Gadolinium enhancing lesions could be registered in 5 patients before initiating therapy, after the first two courses of rituximab only one patient showed inflammatory MRI lesions. In three patients paraclinical progression was seen on MRI. Adverse effects occurred as mild to moderate infections, no severe adverse effects were reported.

**Conclusion:** In all 15 patients Rituximab reduced inflammatory brain lesions, clinical relapses and showed a stabilizing of EDSS and paraclinical progression. No severe side effect occurred within an observation phase of 24 up to 224 weeks. Although the patient population is small and heterogenous the positive results of previous studies regarding efficacy can be confirmed. Furthermore, this is to our knowledge the first report showing that the standard dosing protocol as single infusions according to the B-cell return might be effective as well and safe.

**Background:** Fingolimod is on the market for relapsing remitting MS in Germany since April 2011. Fingolimod is indicated as an escalating therapy in active relapsing remitting MS where interferon beta failed and as a first line therapy in severe exacerbations.

**Objective:** The aim of the study is to analyse data of efficacy and safety of Fingolimod in a daily life MS population.

**Methods:** Since license in the Berlin JKB MS Center 95 (8%) out of 1201 MS patients started fingolimode. Data of all MS patients were documented prospectively in our data base MDOC.

**Results:** Mean age of the 95 patients (64 f, 31 m) was 42.8 ys (18–68), mean duration 17.2 ys (1–38), mean EDSS 4.1 (0-7.0), mean annual relapse rate 0.81 (0-4)), mean number of pretreatments 4.0 ( n 39 natalizumab, n 17 mitoxantrone). So far no cardiac toxicity was observed, no severe infections, no skin tumors. There was no negative effect on concomittant diseases like psoriasis, colitis, diabetes type 1 .15 patients discontinued therapy for different reasons. 40 patients were more than 12 and 78 more than 6 months on drug. The efficacy concerning relapse activity, progression and MRI activity will be analysed with end of July 2012 and data will be presented.

**Conclusion:** In the daily practice our one year experience with fingolimode in 95 patients is so far according to the study results, despite the fact that our patients differ from the study population concerning pretreatments, EDSS, duration of disease and concomittant diseases.

**P-96**

**Rationale And Design Of PERFORMS: An Observational Study To Evaluate The Effectiveness, Safety and Effect On Health Related Quality Of Life Of Fingolimod Treatment In Routine Practice**

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**Background:** Safety and efficacy of fingolimod in relapsing-remitting multiple sclerosis (MS) patients was successfully demonstrated in the phase III clinical program.

**Objective:** The PERFORMS study explores the effect of fingolimod, in relation to other disease modifying treatments (DMT), on health-related quality of life (QoL) through patient reported outcome measures. It assesses the effectiveness of fingolimod, and describes physician impression of treatment with fingolimod in routine clinical practice.
Methods: This is a non-interventional, multi-center, open-label, prospective study, enrolling approximately 250 patients at 25 sites across Europe, South East Asia and the Middle East. Patients observed are adults with MS, receiving either fingolimod 0.5 mg or other approved MS DMTs, as part of routine medical care. Patients are followed for 12 months +/-4 weeks. Evaluations are determined by the treating physician according to the local prescribing information and in accordance with standard of care and individual clinical practice. Patient reported outcome is assessed with Multiple Sclerosis International Quality of Life Questionnaire, MusiQoL, which is a validated, multi-dimensional, self-administered, disease-specific questionnaire. The questionnaire consists of 31 items assessing nine dimensions of health-related QoL relevant to MS patients. The survey is completed by patients at baseline, Month 6, and Month 12/end of study.

Results: The study was initiated in March 2012 and final patient visits expected in January 2015, with results anticipated in mid-2015.

Conclusions: The PERFORMS study is conducted to expand the knowledge of fingolimod treatment and explore the effect of the drug on patients’ health related QoL in real-world clinical practice.

P-97
GILENYA RISK AND SUPPORT PROGRAM. A MELBOURNE BASED EXPERIENCE OF A RISK MANAGEMENT PROGRAM
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Introduction: Multiple Sclerosis is a complex neurological disease. The recent introduction of new therapeutic agents provides more options for treatment of MS; however, many of these options have safety concerns.

Background: To ensure the safe and effective use of these treatments rigorous and thorough risk management programs (RMP) are required. These programs are the mutual responsibility of government bodies, pharmaceutical companies and health care providers. The goal of any RMP is to protect our patients and in doing so provide the best possible health outcomes.

Methods and Results: Our centre in Melbourne developed the GRASP (Gilenya® Risk and Support Program) in response to the introduction of fingolimod (Gilenya®) in Australia in 2011. This program comprehensively monitors and supports patients whilst on fingolimod and through the screening process. This poster provides an overview of the GRASP program and the key features of the program. We also detail our experience of initiating Gilena therapy to more than 200 people with MS in Melbourne, including details of our protocol and profile of the adverse events we observed.

Conclusions – work in progress: Our study demonstrates that there were very few unanticipated safety concerns with Gilenya®. Adherence to the medication and to the follow-up protocol were also identified as risks, and our study demonstrated good adherence to the medication, however poor adherence to follow protocols for monitoring the safety risks.

P-98
Effect of BG-12 (Dimethyl Fumarate) in Subgroups of Patients with Relapsing–Remitting Multiple Sclerosis: Findings From Two Phase 3 Studies (DEFINE and CONFIRM)
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Background: In the Phase 3 DEFINE and CONFIRM studies, BG-12 (dimethyl fumarate) significantly reduced relapses over 2 years versus placebo in relapsing–remitting multiple sclerosis (RRMS) patients.

Objective: To report efficacy of BG-12 in patient subgroups from DEFINE and CONFIRM.

Methods: Patients were randomised to oral BG-12 240 mg twice (BID) or three times daily (TID), placebo, or glatiramer acetate (reference comparator; CONFIRM only). Primary endpoints at 2 years were the proportion of patients relapsed (DEFINE) and annualised relapse rate (ARR; CONFIRM). Effects on relapses were evaluated in pre-specified patient subgroups stratified by
Efficacy and Safety of BG-12 (Dimethyl Fumarate) in Relapsing–Remitting Multiple Sclerosis in the Phase 3 CONFIRM Study

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Background: In a Phase 3 study (DEFINE), oral BG-12 (dimethyl fumarate) showed significant efficacy and an acceptable safety profile over 2 years in relapsing–remitting multiple sclerosis (RRMS) patients.

Objective: To describe the efficacy and safety of BG-12 in the Phase 3 CONFIRM study.

Methods: Patients with RRMS (McDonald criteria 2005) and Expanded Disability Status Scale (EDSS) score 0–5.0 were randomised to BG-12 240 mg twice (BID) or three times daily (TID), glatiramer acetate (GA) 20 mg/day (reference comparator) or placebo. Endpoints included annualised relapse rate (ARR), disability progression, and magnetic resonance imaging (MRI) assessments in a subset of patients, at 2 years. Safety assessments included adverse event (AE) monitoring and laboratory tests.

Results: 1,417 randomised patients were dosed. ARR was significantly reduced at 2 years by 44% (BG-12 BID; p=0.0001), 51% (BG-12 TID; p=0.0001) and 29% (GA; p=0.0128) versus placebo. Risk of 12-week confirmed disability progression was reduced by 21%, 24% and 7% with BG-12 BID, TID and GA versus placebo, although it was not statistically significant. In the MRI cohort (n=681), all active treatments significantly reduced brain lesion activity versus placebo. Overall incidence of AEs and serious AEs was similar across groups. The most common AEs occurring more frequently with BG-12 than placebo were flushing and gastrointestinal events. No opportunistic infections or malignancies were reported in BG-12 groups.

Conclusion: Positive efficacy and safety results, consistent with results from DEFINE, further support BG-12’s potential as a valuable oral treatment option for relapsing MS.

P-100 (O-36)
Therapeutic effect of co-administration of Amantadine and Aspirin on fatigue in patients with multiple sclerosis: a randomized placebo-controlled double-blind study

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Background: Fatigue is recognized as one of the most disabling and frequent symptoms of multiple sclerosis (MS). Amantadine appears to have some proven ability to alleviate the fatigue in MS. The aim of this study was to assess the efficacy of co-administration of amantadine and aspirin for the treatment of fatigue in multiple sclerosis.

Methods: Forty-five ambulatory patients aged 20–50 years with a diagnosis of MS, a stable disability level ≤6 on the Kurtzke extended disability status scale (EDSS), and a mean score ≥4 on the fatigue severity scale (FSS) were eligible for the 6 weeks, randomized placebo-controlled double-blind study. Efficacy was evaluated by self rating scales, using the FSS. Data analysis was performed by T test, chi-square test,
Effects of Melatonin on Visual Functioning of patients with Multiple Sclerosis
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Background: Several clinical studies suggest that melatonin is a neuroprotective molecule in neurodegenerative disorders and it showed to be reduced in Multiple Sclerosis (MS) patients.

Objective: To assess the influence of Melatonin supplementation on visual characteristics in patients with MS.

Methods: In a Quasi Experimental plan, 24 patients with MS were asked to voluntarily participate in the study. All subjects were taking their routine medications. Visual functioning was evaluated using Visual Functioning Questionnaire (VFQ-25) and standard pattern reversal Visual Evoked Potentials (VEP) records. Serum Melatonin levels were also measured using an ELISA assay, first, 2 hours after morning wake up, then a single dose of 3 mg Melatonin was orally administered. After 50 min, VEP and second blood sample were taken. In a pretreatment 2 weeks course, patients were asked to take Melatonin every night for 14 days and third blood sampling. VEP-25, VEP were repeated again at the day 16th after 24 hours of Melatonin wash out.

Results: In all subjects, Serum Melatonin levels were enhanced only in the second blood samples while no significant differences were found between the first and third taken samples. Second VFQ scores showed significant improvement. VEP latencies of one or two eyes were also reduced in all subject both in second and third records.

Conclusions: Our findings suggest significant improvements of visual symptoms of MS after daily intake of 3 mg Melatonin. The results calls for further studies and clinical trails before asking all MS patients to take Melatonin supplement every night.

P-102
Effects of Melatonin on Dominant Hand Dexterity of patients with Multiple Sclerosis
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Background: Several clinical studies suggest that melatonin is a neuroprotective molecule in neurodegenerative disorders and it showed to be reduced in Multiple Sclerosis (MS) patients. MS also results in clumsiness and reduced dexterity of distal fine motor performance of the hands.

Objective: To assess the influence of Melatonin supplementation on dominant hand dexterity in patients with MS.

Methods: In a Quasi Experimental plan, 24 patients with MS were asked to voluntarily participate in the study. All subjects were taking their routine medications. Dexterity of dominant hands was evaluated by the O’Connor Tweezers Dexterity Test (OTDT). Serum Melatonin levels were also measured using an ELISA assay, first, 2 hours after morning wake up, then a single dose of 3 mg Melatonin was orally administered. After 50 min, OTDT and second blood sample were taken. In a pretreatment 2 weeks course, patients were asked to take Melatonin every night for 14 days and third blood sampling and OTDT were repeated again at the day 16th after 24 hours of Melatonin wash out.

Results: In all subjects, Serum Melatonin levels were enhanced only in the second blood samples while no significant differences were found between the first and third taken samples. Second OTDT scores were slightly higher but statistically significant improvement were recorded when the third OTDT scores compared with the first one.

Conclusions: Our findings suggest significant improvements of hand motor performance and dexterity in MS after daily intake of 3 mg Melatonin. The results calls for further studies and clinical trials before asking all MS patients to take Melatonin supplement every night.

P-103
Effects of Pilates in Multiple Sclerosis
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**Background:** Pilates is a popular method in the general population. However, the effects of Pilates on balance, mobility and muscle strength in patients with Multiple Sclerosis (MS) have not been investigated before.

**Purpose:** To investigate the effects of Pilates on balance, mobility and muscle strength in ambulatory patients with MS.

**Material and Method:** Twenty five ambulatory female patients with MS were included to the study. Eighteen patients underwent Pilates two times in a week for eight weeks. Seven patients were given a home program for eight weeks as a control group. Balance (Berg Balance Scale), mobility (Timed “Up and Go” test), upper and lower extremity muscle strength (hand-held dynamometer) were assessed.

**Results:** Balance, mobility, upper and lower extremity muscle strength were significantly improved in Pilates group (p<0.05). There was no significant improvement found in all assessed parameters in control group (p>0.05).

**Conclusions:** Pilates may improve balance, mobility and muscle strength in ambulatory patients with MS. Therefore Pilates may be used as a multidimensional therapeutic approach in these patients.

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**P-104**

**Effects of the Clinical Ai-Chi on strength, balance and walking performance in patients with Multiple Sclerosis**

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**Background:** Even Multiple Sclerosis (MS) patients often referred to the aquatic physical therapy, the evidences for this field are not enough. The Clinical Ai-chi seems a new and promising program for MS patients.

**Purpose:** To investigate the effects of the Clinical Ai-Chi on strength, balance and walking performance in ambulatory patients with MS.

**Material and Method:** Eighteen ambulatory female patients with MS (according to Kurtzke Expanded Disability Status Scale scores between 1 and 3.5) were included to the study. Patients were divided into two groups as Ai-Chi and control. Ai-Chi group (n=11) underwent 16 sessions of Clinical Ai-Chi program in a swimming pool, abdominal breathing and active extremity exercises were given as home exercises for the control group (n=7) two times in a week for eight weeks. Following measurements were used for assessment respectively; Hand-held dynamometer for upper and lower muscle strength, duration of single leg stance for balance, Timed up and go test for mobility, Activities-Specific Balance Confidence Scale for the level of perceived confidence and 6 minute walk test (6MWT) for walking performance. Outcome measurements were done before and after intervention.

**Results:** While improvements were observed in upper and lower extremity muscle strength, balance and walking performance in the Ai-Chi group (p<0.05) no improvements were found in the control group (p>0.05) between before and after the intervention.

**Conclusions:** According to these findings, the Clinical Ai-Chi may improve upper and lower extremity muscle strength, balance and walking performance in patients with MS.
Results: While fatigue and mood were improved (p<0.05), the quality of life was not improved significantly (p>0.05) in Ai-Chi group. Fatigue, mood and quality of life were not significantly improved in control group (p>0.05).

Conclusions: These results showed that Ai-Chi might be useful for reducing fatigue and improving mood in patients with MS.

Poster Session 8

Treatment for NMO

P-106
Plasma Exchange In Acute Relapses of Neuromyelitis Optica Spectrum Disorder
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Background: Neuromyelitis optica (NMO) and its spectrum disorders (NMOSD) is an autoimmune, inflammatory disorder selectively involving the optic nerve and spinal cord. Acute attacks are treated with pulsed steroids or plasmapheresis (PLEX) rescue therapy in steroid-refractory attacks.

Objective: To describe the clinical outcomes and complications of PLEX-treated attacks in NMO/NMOSD.

Methods: We retrospectively reviewed all treated attacks in NMO/NMOSD between May 1991 and May 2011 at the National Neuroscience Institute, Singapore. We measured change in Expanded Disability Status Score (EDSS) overall, visual acuity and colour vision for optic attacks and motor/sensory/bladder/bowel dysfunction for spinal attacks, at baseline, attack nadir, immediately and 6 months post-PLEX. Clinical improvement was quantified as nil/mild/moderate/marked.

Results: Sixteen attacks (10 optic neuritis, 4 transverse myelitis, 2 opticospinal) in 10 patients (6 NMO, 4 NMOSD; 7 NMO-IgG seropositive) were analysed. The average time to PLEX initiation was 8.94 days (range 2-38) post-steroid initiation; average number of cycles was 5 (IQR=4.5-6). Twelve of 16 (75%) attacks showed clinical improvement: 6 marked, 1 moderate and 5 mild. EDSS improved in 43.8% (7/16) of attacks. NMO-IgG seropositivity was associated with clinical improvement (OR=24, 95%CI=1.02-560.2, p=0.071). At 6 months, 7/16 attacks improved back to baseline, 13/16 attacks improved to better than nadir. Complications were reported in 11 attacks; the commonest being hypotension (n=7). There were no fatalities.

Conclusions: PLEX treatment in NMO/NMOSD attacks produces functional and clinical improvement, especially for NMO-IgG seropositive patients. Marked improvement occurred in up to a 38-day delay of PLEX.

P-107
Plasma Exchange for Steroid-Refractory Optic Neuritis in Neuromyelitis Optica
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Background: Neuromyelitis optica (NMO) is an autoimmune, inflammatory disorder characterised by severe and selective involvement of the optic nerve and spinal cord. Acute NMO attacks are treated with pulsed steroids or plasmapheresis (PLEX) rescue therapy in steroid-refractory attacks.

Objective: To compare the outcomes of PLEX-treated with pulsed steroids-treated NMO-optic neuritis (ON) attacks.

Methods: We retrospectively reviewed all treated NMO-ON attacks between May 1991 and May 2011 at the National Neuroscience Institute, Singapore. We measured change in visual-acuity (VA) and colour-vision (CV) from baseline vision and visual nadir, up to 6 months after attack. To determine whether PLEX had any additional benefit, we compared PLEX-treated attacks with steroid-refractory attacks.

Results: Twenty-two patients (33 eyes; 58 attacks) were analysed; 27.6% (16/58) of attacks were treated with intravenous methylprednisolone (IVMP) followed by PLEX; the rest had IVMP only. Evaluating initial response to IVMP, 6.3% (1/16) IVMP-PLEX-treated attacks compared to 45.2% (19/42) IVMP-only treated attacks had improved VA; 23 IVMP-only treated attacks were steroid-refractory. Following IVMP-PLEX treatment, 87.5% (14/16) had improved VA; 25.0% (4/16) had improved CV. At 6-months, 93.8% (15/16) IVMP-PLEX-treated attacks compared to 82.6% (19/23) steroid-refractory attacks maintained/improved VA over visual nadir (OR=3.16, 95%CI=0.32-31.29, p=0.384); 43.8% (7/16) vs 13.0% (3/23) maintained/improved VA over baseline vision (OR=5.19, 95%CI=1.09-24.79, p=0.05). Complications were
reported in 81.3% (13/16) of PLEX treatments; hypotension being the commonest (n=5). There were no fatalities.

Conclusions: Patients with NMO-ON attacks improve regardless of treatment, but PLEX significantly improve VA up to 6 months post-treatment. Administrators of PLEX must be aware of the potential treatment complications.

P-108 (Retracted)

P-109  
**Long-term Azathioprine Therapy for Neuromyelitis Optica:A 9-year Follow-up Study**  
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**Background:** No treatment with sufficient evidence to prevent relapses of neuromyelitis optica (NMO) has been established yet.

**Objective:** We encountered a case of NMO in which relapses could be well-controlled by long-term azathioprine therapy.

**Case:** A 59-year-old Japanese man first experienced uncontrollable hiccups 13 years earlier. Three years later, he presented with right hemiparesis and MRI lesions in the left internal capsule and midbrain. Three months later, gait disturbance developed, along with a longitudinally extensive lesion from the third to the seventh cervical spinal cord segments on MRI. Symptoms improved following high-dose intravenous methylprednisolone (IVMP) therapy. Two months later, hiccups appeared again, along with a sensation of tightness of the trunk; IVMP proved effective. Interferon-beta (IFN-β)-1b was started. However, consciousness disturbance, visual impairment and tetraplegia occurred, with CSF pleocytosis; two longitudinally extensive lesions in the cervical and thoracic cord were observed on MRI. Two courses of IVMP therapy were partially effective. IFN-β-1b was discontinued because of worsening NMO. Nine years ago, paraplegia and a longitudinally extensive cervical cord lesion appeared. The following month, the patient was referred to our hospital. Right optic atrophy was observed. Oral administration of azathioprineAZP (100 mg/day) was started following IVMP. His clinical features satisfied the diagnostic criteria for NMO. Anti-aquaporin-4 antibody was detected in the serum. We followed the patient for 9 years after the start of azathioprineAZP therapy, and no relapse of NMO was detected.

**Conclusion:** Our findings indicate that azathioprineAZP therapy might be effective in suppressing relapses and achieving long-term remission in NMO patients.

P-110  
**Interferon beta may induce cerebral lesions in non-multiple sclerosis inflammatory demyelinating diseases**  
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**Background:** The spectrum of idiopathic inflammatory demyelinating diseases (IDDs) encompasses multiple sclerosis (MS), its variants and other entities including neuromyelitis optica (NMO) and acute disseminated encephalomyelitis (ADEM). Although Interferonβ (IFNβ) is the first-line therapy for MS, the outcome of IFNβ treatment in patients with non-MS IDDs is controversial.

**Objective:** To investigate the clinical and MRI changes in Chinese patients with non-MS IDDs after IFNβ therapy.

**Methods:** Fourteen patients with non-MS IDDs, including 7 NMO, 4 NMO spectrum disorder (NMOSD) and 3 multiphase ADEM (mADEM), were retrospectively enrolled from our MS demyelinating diseases database of Sun yat-sen University from 2006.01-2012.01. Patients demographic data, clinical features, MRI characteristics prior to and post IFNβ therapy were compared and analysed.

**Results:** All cases with NMO, NMOSD and mADEM showed worsening of clinical symptoms post IFNβ therapy ranging from 3 to 6 months. Heterogeneous atypical cerebral lesions were developed in cerebral white matter, brain stem and cerebellum, with some lesions mimicking MS lesions in the lesion location and configuration. mADEM with negative NMO-IgG may be exacerbated by IFNβ in clinical and MRI features.

**Conclusions:** IFNβ may induce cerebral lesions in non-MS IDDs, including NMO, NMOSD, and mADEM with negative NMO-IgG.

P-111  
**Inefficient or even Deleterious effects of Interferon beta-1a on Neuromyelitis Optica**  
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2 Department of Neurology, PLA General Hospital ,
Background: Interferon beta-1a (IFNβ-1a) and Natalizumab are two of the first-line disease-modifying drugs that used to treat MS. However, whether they are effective or inefficient for neuromyelitis optica remains controversial.

Objective: To evaluate effects of Interferon beta-1a (IFNβ-1a) and Natalizumab on Neuromyelitis optica (NMO).

Methods: We retrospectively analyzed four Chinese Neuromyelitis optica (NMO) patients treated with Interferon beta-1a (IFNβ-1a) and one of them followed by Natalizumab treatment. IFNβ-1a was used (three times a week, subcutaneous injection) for 6 months to 24 months respectively and all cases meet the Wingerchuk 2006 criteria of NMO.

The number of relapsing in patients with NMO was compared before and after IFNβ-1a treatment. All patients had cerebral and spinal MRI on one or more occasions and AQP4 antibody in 3 patient serum samples were detected with indirect immunofluorescence in human AQP4 transfected cells.

Results: the number of relapses was increased in 3 patients after IFNβ-1a treatment, while no significant improvement was seen in 1 patient. One patient who failed to improve after IFNβ-1a treatment was proved ineffective with Natalizumab. Our results suggest that IFN-β1a and Natalizumab may be inefficient in the treatment of NMO.

Conclusion: The disease modifying treatment (such as IFNβ-1a and natalizumab) is usually inefficient or even deleterious in patients with NMO.

P-112
Failure of Interferon beta-1a and Natalizumab to Prevent Relapses in Neuromyelitis Optica
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We report 4 Chinese Neuromyelitis optica (NMO) patients treated with Interferon beta-1a (IFNβ-1a) and one of them followed by Natalizumab treatment. The number of relapses in patients with NMO was compared before and after the treatment. Results indicated that the number of relapses was increased in 3 patients after IFNβ-1a treatment, while no significant improvement was seen in 1 patient. One patient who failed to improve after IFNβ-1a treatment was proved ineffective with Natalizumab. Our results suggest that IFN-β1a and Natalizumab may be inefficient in the treatment of NMO.

P-113
Preliminary Study of Efficacy and Safety of Mitoxantrone for the Treatment of Relapsing NMO
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Background: Neuromyelitis optica is a severe demyelinating disease that affects preferentially the optic nerve and spinal cord but usually spares the brain. Pathologic and serologic data support a B-cell–mediated pathogenesis. Mitoxantrone hydrochloride (MX), approved for worsening relapsing-remitting and secondary progressive multiple sclerosis, has been shown to induce an inhibitory effect on humoral autoimmunity.

Objective: To evaluate the benefit of mitoxantrone in patients with relapsing neuromyelitis optica spectrum disorders (NMOSD).

Methods: Seven patients with recurrent NMOSD were enrolled for the treatment. Of which, four satisfied the diagnostic criteria of NMO, and three belonged to NMOSD. The patients were treated with MX (12 mg/m² intravenously) every 3 months for 2 years. The numbers of relapses and expanded disability status scale (EDSS) score were used as outcome measures.

Results: Mean duration before treatment was 4.27±4.75 (1.2-14) years. Mean total dosage was 79.5±17.89 mg/m². In the 7 patients, 5 patients completed two years of therapy, 2 patients completed one year of therapy. There was significant difference in the mean annual relapse rates (ARR) [before 2.03±1.24; on MX 0.43±0.45 (P=0.028)], and EDSS score [before 6.29±1.58, post 5.07±1.96, (P=0.027)] in the series of patients. The outcomes showed significant benefit in these patients. During MX treatment, three patients became relapse free. The adverse events noted were transient leukopenia, nausea, alopecia, menstrual disorders, urinary-tract infection. Three patients relapsed within the following one year after MX therapy.

Conclusions: Our results suggest a beneficial effect of mitoxantrone treatment for relapsing NMOSD. But when and how to maintain the immunosuppressive effect after MX therapy remains a problem.

Poster Session 9
Experimental Studies for Demyelinating Disease
Investigation on expressions of AQP-4 and CD4+ CD25+ regulatory T cells in EAE
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Objective: Experimental allergic encephalomyelitis (EAE) was induced in female C57BL/6 mice with the extracellular domain of myelin oligodendroglia glycoprotein (MOG1gd). Percentages of CD4+ CD25+ T cell (Treg) were tested, and also the expression of AQP-4.

Methods: Molecular cloning technology was used to produce MOG1gd fusion protein. The MOG1gd-TrxA fusion protein and TrxA protein were purified by metal chelate affinity chromatography (MCAC). Mice were injected s.c. in the flank with 300 Lg MOG1gd in complete Freund’s adjuvant (CFA) supplemented with 4 Lg/LMt. H37Rv. Mice received 0.4 ml emulsion of spinal cord homogenate of guinea pigs (GPSCH) in positive control group, and the same volume emulsion of TrxA in negative control group. Clinical scores and histopathology were evaluated. Immunochemistry and real-time PCR were performed to test level of AQP-4.

Results: Mice in both MOG group and GPSCH group were shown chronic non-remitting course. The onset of disease, the time point for appearance of the most severe clinical symptoms and the clinical score between the two groups were in no significant differences (P >0.05). However, animals in the TrxA treated group did not exhibit clinical signs of EAE. Histologic sections of the brain and spinal cord taken from affected animals were shown by perivascular infiltration of mononuclear cells, gliosis, and multifocal demyelination. Lesions scattered throughout the entire nervous system (CNS) including brainstem, spinal cord, cerebellum, and periventricular white matter. There were significant differences between MOG group and TrxA group in the level of lesion-centric AQP-4 expression shown up by immunohistochemistry and real-time PCR (P < 0.05). Percentages of CD4+CD25+ T cells in MOG group and GPSCH group were (4.71 ± 1.61)% and (1.44 ±0.165)%, respectively, both of which were significantly lower than that in TrxA treated group (P < 0.01). The difference between MOG group and GPSCH group was also of statistical meaning (P < 0.01).

Conclusion: EAE induced in C57BL/6 mice with MOG1gd is reproducible. It shares the similar clinical signs and pathologic features with humanMS. Thus, we find a good way to further study the immune mechanisms of MS and also to search for the effective treatments. Expression of AQP-4 in EAE animals is correlated with the severity inflammatory infiltration.

Curcumin Suppressing the Expression of RGMa and Promoting Axonal Regeneration in EAE Mice
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Backgrounds: Repulsive guidance molecule a (RGMa) is one of the most potential reported neurite growth inhibitors. Curcumin is a naturally occurring polyphenolic phytochemical and can reduce the clinical severity of experimental autoimmune encephalomyelitis (EAE) model of multiple sclerosis (MS). But the effect of curcumin on RGMa and axonal regeneration in EAE and MS remains unclear.

Objective: Our aim is to observe the effect of curcumin on suppressing the expression of RGMa and promoting axonal regeneration in EAE.

Methods: EAE was induced in myelin oligodendrocyte glycoprotein (MOG)-induced female C57 bl/6 mice. Curcumin was orally administered to the mice at 200 mg/kg daily from days 0 to 14 after immunization. Mice in the control group were received equal volume of 0.5% methylcellulose solution. The neurologic function was evaluated by EDSS score. Neurofilament protein 200 (NF-200) was used to assess axonal regeneration. The expression of RGMa and NF-200 were observed by immunofluorescence and western blot.

Results: Neurological function in curcumin group was significantly improved (p < 0.05). RGMa was greatly increased after EAE induction compared with normal group but was significantly decreased in curcumin group (p < 0.01). The axonal were disorderly arranged and became shorter and fewer in control group, but were neatly aligned, with long NF-200 positive fibers in curcumin group (p < 0.01).

Conclusions: Curcumin can inhibit the expression of RGMa and promotes axonal regeneration in EAE mice. The axonal regeneration effects probably mediated partly through suppressing the expression of RGMa.

The Neuroprotective Potiental Of SEA From
Schistosoma Japonicum On EAE Except For Its Th2-biased Immune Response
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Background: Soluble egg antigen (SEA) is strongly antigenic and inherently induces Th2-biased immune responses. We successfully found that SEA from Schistosoma japonicum is able to ameliorate the severity and progression of experimental autoimmune encephalomyelitis (EAE) through the mechanism of Th2-shift immune response. Previous studies have shown that Th2 cells and cytokines may increase the expression of neurotrophins (NTs) and NTs has the ability of immune regulation to enlarge the Th2 response.

Objective: To prove that if SEA-induced Th2 response has the neuroprotective immunological effect on EAE. That is to say, SEA-induced Th2 response may increase the expression of NTs and this increment in turn may further enlarge the Th2 response induced by SEA, which makes a positive regulatory circle.

Methods: Splenocytes from SEA- or PBS-preimmunized C57BL6/J mice were cultured in vitro. Expressions of Nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and Th2 cytokines were measured by ELISA, Western blot and flow cytometry. Exogenous Th2 cytokines and their antibodies were used to test if they can augment or reduce NTs’ expressions. Supernatants of splenocytes were cocultured with PC12 cells to observe the axonal growth.

Results: Expressions of NTs were increased in SEA-preimmunized mice compared with PBS controls. Their expressions were increased with exogenous Th2 cytokines and decreased with antibodies of Th2 cytokines. Axonal growth of PC12 was obvious in SEA-preimmunized supernatants.

Conclusions: SEA may have the neuroprotective potential beyond its Th2-biased immune response and such shifting response may augment its neuroprotective ability.

P-117
Role Of Rho Kinase For Neurite Outgrowth And Synapse Formation In Multiple Sclerosis
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Background: Rho kinase (ROCK) may participate in the impairment of neurons and the inhibition of synapse formation in multiple sclerosis (MS). And the ROCK inhibitor could promote the neuritogenesis and the stem cell mobilization.

Objective: To explore the role and mechanism of ROCK for neurite outgrowth and synapse formation in MS.

Methods: ROCK activity of MS serum was measured by ELISA kit. MS serum treated with or without ROCK inhibitor Fasudil was co-cultured with mouse primary neurons for observing its effect to neurons. Brain and spinal cord from EAE mice treated with Fasudil were used to detect whether peripheral administration can influence central nervous system.

Results: The activity of ROCK was elevated in MS serum compared with healthy control. When MS sera were added into cultured neurons, the viability of neurons was impaired, the neurite outgrowth was shortened and the expression of synaptophysin was declined. MS sera treated with Fasudil in vitro improved the synapse formation, accompanied by elevated synaptophysin. Fasudil alleviated the severity of symptom and delayed onset in EAE. The brain and spinal cord of EAE mice treated with Fasudil promoted the synapse formation, accompanying with the reduction of CRMP-2 phosphorylation. Fasudil treatment in vivo lessened the inhibitory effect of MS serum to the synapse formation in primary neurons.

Conclusions: Activated ROCK in MS serum and protein extract from EAE mice suppresses the synapse formation in primary neurons. Inhibition of ROCK in vitro and in vivo improves clinical score and promotes the synapse formation.

P-118
Estrogen Inhibits Estrogen Receptor(ER)-α-mediated Rho-kinase Expression in Experimental Autoimmune Encephalomyelitis Rats
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Backgrounds: An Anti-inflammatory and neuro-protective effect of estrogen on multiple sclerosis (MS) has been reported in previous studies. Evidences are found that estrogen can inhibit axonal loss in MOG-induced experimental autoimmune...

**Objective**: To explore the effect of estrogen on ROCK in EAE rats and to explore the probably mechanism that estrogen promotes axonal regeneration through the inhibitory of ROCK.

**Methods**: Ovariectomized female wistar rats were treated with daily injections of 17β-estradiol (E2), E2 plus non-selective ER antagonist ICI 182780, ERα-selective ligand agonist propyl pyrazole triol (PPT), ERβ-selective ligand WAY-202041, or PBS respectively. The neurologic function was evaluated by EDSS score. Neurofilament protein 200 (NF-200) was used to assess axonal regeneration. The expression of ROCK and NF-200 were tested by immunohistochemistry and western blot.

**Results**: E2 can significantly improve neurological function in EAE rats. E2 inhibited the expression of ROCK and increased the expression of NF-200. The inhibitory effect on ROCK was abolished when ICI 182780 was added to E2. Furthermore, PPT decreased the expression of ROCK. WAY-202041 had no effect on the expression of ROCK.

**Conclusions**: Estrogen inhibits the expression of ROCK in EAE rats and promotes axonal regeneration through the inhibitory of ROCK. The inhibitory effects are mediated by ERα but not ERβ.

**P-119**

**Immune-related GTPase Irgm1 exacerbates experimental auto-immune encephalomyelitis by promoting the disruption of blood- brain barrier and blood-cerebrospinal fluid barrier**

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**Abstract**

Experimental autoimmune encephalomyelitis (EAE), the animal model of multiple sclerosis (MS), is a T cell–mediated autoimmune condition characterized by prominent inflammation in the CNS. In this model, autoreactive T cells are primed in peripheral lymph nodes and migrate into uninfamed CNS across blood-cerebrospinal fluid barrier (BCSFB) and blood-brain barrier (BBB) to initiate inflammation. However, the molecular mechanism controlling T cell migration remains to be determined. In an in vivo EAE mouse model, we have shown that Irgm1 (also known as LRG-47), a member of the immunity-related GTPase family, promotes the disruption of both BCSFB and BBB, and exacerbates the phenotypes of MOG-induced EAE. During EAE, Irgm1 was up-regulated in reactive astrocytes, ependymal cells and epithelial cells of the choroids plexus, which, in turn, promotes T cell infiltration into the CNS. Electron microscopy study showed that the MOG-disruption induced in both BBB and BCSFB was protected in the Irgm1−/− mice. Moreover, the expression of Claudin-5 (CLN-5), a major molecular determinant of BBB, in brain microvessel endothelial cells (BMVECs) was decreased in WT EAE mice while increased in Irgm1−/− mice. In addition, the expression of CC-chemokine ligand 20 (CCL-20), an important chemokine mediating lymphocyte trafficking across BCSFB, in the epithelial cells of choroids plexus was significantly suppressed in naïve and EAE-induced Irgm1−/− mice. These data suggest that Irgm1 is an important molecular regulator for the properties of both BBB and BCSFB, and a proinflammatory factor for EAE.

**P-120**

The anti-inflammatory effect of donepezil on experimental autoimmune encephalomyelitis in C57 BL/6 mice

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**Background**: Donepezil is a potent and selective acetylcholinesterase inhibitor. It has been reported to restore cognitive performance in multiple sclerosis (MS) patients and experimental autoimmune encephalomyelitis (EAE) mice, an established model of MS. However, there are no reports about the anti-inflammatory effects of donepezil on EAE.

**Methodology/Principal Findings**: Mice was immunized with myelin oligodendrocyte glycoprotein 35-55 amino acid peptide and donepezil treatment was initiated at day 7 post immunization (7 p.i., subclinical periods, early donepezil treatment) and day 13 p.i.
(clinical periods, late donepezil treatment) with the dosage of 1, 2 and 4 mg/kg/d respectively and the therapies persisted throughout the study. The expression of nerve growth factor (NGF), and its precursor form (proNGF) as well as matrix metalloproteinase-2 (MMP-2) and matrix metalloproteinase-9 (MMP-9) in the brain of EAE mice were detected by Western blot. The results showed that the 2 mg/kg/d late donepezil treatment was thought as the optimal dosage for therapy on EAE and could ameliorate inflammation and demyelination in the spinal cord, and improve the outcomes of magnetic resonance imaging in the brains of EAE mice. In addition, donepezil blocked the reduction of NGF, suppressed the production of proNGF and inhibited the expression of MMP-2 and MMP-9 in the brains of EAE mice.

Conclusions/Significance: Our data suggested that the anti-inflammatory effects of donepezil may be a novel mechanism in treating EAE and further provided further insights to understand the donepezil’s neuroprotective activities in MS.

P-121
Transplantation of Olfactory Ensheathing Cells promotes partial recovery in Experimental Autoimmune Encephalomyelitis
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The goal of this study was to explore whether olfactory ensheathing cells (OECs) were able to promote functional recovery and axonal regeneration when OECs were transplanted to adult Lewis rats with experimental autoimmune encephalomyelitis, which serve as a disease model for multiple sclerosis (MS). OECs were implanted into the rats through the vena caudalis (group A) and the lateral cerebral ventricle (group B). The results showed that the clinical symptoms in the rats in both groups were relieved to various degrees, compared to the control group. However, by using HE and LFB staining, no significant difference was shown in histopathology between the treatment groups and the control group. In conclusion, the beneficial effects found in the present study further support the use of OECs for clinical treatment of MS and other demyelinating diseases.

P-122
The protective effect of berberine against neuronal damage by inhibiting matrix metalloproteinase-9 and laminin degradation in experimental autoimmune encephalomyelitis
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Our previously studies had found that berberine could attenuate the clinical severity of experimental allergic encephalomyelitis (EAE) in C57 BL/6 mice by reducing the permeability of blood–brain barrier, decreasing the expression and activity of matrix metalloproteinase-9, and decreasing the inflammatory infiltration. This study was undertaken to assess the protective effect of berberine against neuronal damage in the brain parenchyma of EAE mice and its mechanism. EAE was immunized with myelin oligodendrocyte glycoprotein 35-55 amino acid peptide and berberine treatment was initiated at the day of disease onset and the medication was administered daily until mice were sacrificed. In the terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling (TUNEL) assay, berberine reduced TUNEL-positive neuronal cells of EAE mice. Gelatin gel in situ gelatin zymography showed upregulation of gelatinase activity, which mainly located in neurons and colocalized with remarkable laminin degradation in EAE mice. Berberine significantly inhibited gelatinolytic activity in gel zymography and in situ gelatin zymography and reduced the laminin degradation in EAE mice. Our data suggest that berberine may provide a protection against neuronal damage in EAE by inhibiting gelatinase activity and reducing laminin degradation. These findings further supported that berberine might be a potential therapeutic agent for multiple sclerosis.

P-123
IFN-γ signaling in astrocytes and microglia has opposite effects in CNS autoimmunity
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Artemisinin attenuates lipopolysaccharide-stimulated proinflammatory responses by inhibiting NF-κB pathway in microglia
cells

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Microglial activation plays an important role in the pathogenesis of demyelination in multiple sclerosis (MS). Inhibition of microglial activation in the CNS of MS patients has become a new focus of research, which may contribute to the development of new therapeutic strategies. Recent studies have indicated that the antimalarial agent artemisinin has the ability to inhibit NF-κB activation. In this study, the inhibitory effects of artemisinin on the production of proinflammatory mediators were investigated in lipopolysaccharide (LPS)-stimulated primary microglia. Our results show that artemisinin significantly inhibited LPS-induced production of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), monocyte chemotactic protein-1 (MCP-1) and nitric oxide (NO). Artemisinin significantly decreased the mRNA levels of these pro-inflammatory cytokines and inducible nitric oxide synthase (iNOS) and increased the protein levels of interleukin-1β (IL-1β) and IL-6. Our results suggest that artemisinin is able to inhibit neuroinflammation by interfering with NF-κB signaling. The data provide direct evidence of the potential application of artemisinin for the treatment of MS.

P-125
Efficient gene transfection in the neurotypic cells by star-shaped polymer consisting of β-cyclodextrin core and poly (amidoamine) dendronarms

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In order to find the effective vectors that had higher transgene expression to the neuronal cells, we tested the star-shaped polymer consisting of β-cyclodextrin core and poly (amidoamine) (PAMAM) dendron arms [β-CD-(D3)a] as the vector to transfect the neuronal cells because of its high transfection efficiency and low cytotoxicity. In this study, the physicochemical properties of the β-CD-(D3)a/plasmid DNA (pDNA) complexes were characterized by using gel electrophoresis, dynamic light scattering, transmission electron microscopy and zeta-potential experiments. Among the human embryonic kidney 293 cells (HEK
293 cells) and human neuroblastoma SH-SY5Y cells, β-CD-(D3)_3/pDNA complex demonstrated a lower toxicity compared to those of PAMAM/pDNA complex. When the N/P ratio was over 20, it was observed that PAMAM had a faster increment in toxicity compared to β-CD-(D3)_3. Fluorescent image, confocal microscopy image and flow cytometry showed that β-CD-(D3)_3/pDNA complexes had significantly higher transgene activity than that of PAMAM/pDNA in the two kinds of cells. For example, in the SH-SY5Y cells, the transfection efficiency was 20% and 7.5% for β-CD-(D3)_3/pDNA and PAMAM/pDNA complexes, respectively. These results indicated that might be a promising candidate for neurotypic cells gene delivery with the characteristics of good biocompatibility, relatively high gene transfection efficiency and potential in vivo gene delivery ability.

P-126
Imaging optic nerve and spinal cord lesions in myelin antigen TCR transgenic mice with high-field rodent MRI
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Purpose: Neuromyelitis optica (NMO), an inflammatory demyelinating disease with poor prognosis, predominantly affects optic nerves and spinal cord. Differential diagnosis between NMO and multiple sclerosis (MS), particularly at the early stage of disease, constitutes a clinical dilemma due to the similarity between NMO and optic-spinal MS, and such differential diagnosis is instrumental for management of these two diseases as disease progression in NMO is more prominent. In order to compare pathophysiological parameters between the NMO and MS it is important to have research tools that will help to elucidate the specifics of each disease. Methods: Coupled with high-field-strength magnetic resonance imaging (MRI) and immunohistochemistry, we characterized the optic nerve and spinal cord lesions in TCR transgenic mice (referred to as 2D2 mice) in which majority of T cells are biased toward recognizing a human myelin oligodendrocyte glycoprotein epitope, longitudinally. Results: We discovered early BBB breakdown via gadopentate dimeglumine in up to 68% of the 2D2 mice. While the majority of the mice showed little to no brain lesions there is clear evidence of optic nerve and spinal cord inflammation and demyelination. In an attempt to correlate the mice MRI scans with immunohistological staining, we showed the extent of inflammatory infiltrates as well as demyelination that mirrored sites of MRI lesions. Conclusion: This characterization leads us to believe that the 2D2 TCR transgenic mouse would be a helpful model for NMO research.

Poster Session 10
Case Report 10

P-127
Multiple Sclerosis and Nummular Headache
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Abstract: Nummular headache (NH) is a primary headache disorder presenting with mild-to-moderate and pressure like pain in a circumscribed to a rounder elliptical area of approximately 2 to 6 cm in diameter. We report a case of multiple sclerosis (MS) patient with nummular headache. Although in some cases NH can be seen as a comorbid condition of migraine, tension type headache, brain trauma and intracranial mass lesion, but so far as the comorbid condition of MS has not been reported before. To our knowledge, this case is the first submission of MS and NH.

P-128
A case of Multiple Sclerosis and Coeliac Disease
Irkec C1, Batur Caglayan HZ1, Yildirim Capraz1, Dumlu S2, Atalay Akyurek N3

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Objectives: Multiple Sclerosis (MS) is an inflammatory autoimmune disorder of the central nervous system (CNS). Since a correlation between gluten intake and incidence of MS had been reported, the relationship of antigliadin antibodies and MS was debated.
Case Report: We report the case of a 41-year-old female MS patient who is under interferon treatment. After seven years monitoring, during her routine gastroenterological assessment, she was diagnosed with coeliac disease.

Conclusion: Beside the neurological manifestations have been demonstrated in about 10% of Coeliac Disease (CD) patients, white-matter abnormalities in brain MRI are uncommon and controversial. But in literature, MS seems to be associated with CD as in our patient. We suggest that MS patients with gastroenterological complaints should undergo an assessment for CD.

P-129
A case of Marburg’s Variant of Multiple Sclerosis Extensive Demyelination
Chen Y, Wu AM, Hu XQ

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Background: Marburg’s variant of multiple sclerosis is an acute and aggressive atypical form of MS, leading to severe disability or even death several weeks or months after attack. Since Marburg’s first report of this disease, few cases have been described.

Objective: To report a case of Marburg’s variant of multiple sclerosis

Methods: A case report

Results: We report a case of a 63-year-old woman with Marburg’s variant of MS. She quickly became decorticated after 20 days of treatment in other hospital before was transferred to ours. The patient underwent diagnostic brain biopsy and 3 times of magnetic resonance imaging (MRI) several weeks after hospitalization. The pathology of the biopsy revealed a vascular inflammatory cell infiltrate and supported the demyelination of brain. MRI showed extensive white matter involvement in the brain that continuously progressed over time. We administered 3 courses of hormones in high dose, but without significant curative effects.

Conclusions: The prognosis of Marburg is fairly malignant and there is a high death rate.

P-130
Pathologically confirmed tumefactive multiple sclerosis presenting as aphasia
Suk-Won Ahn, Ko-Woon Kim

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Background: Atypical imaging features of multiple sclerosis have been described, which may confound the diagnostic process. These atypical clinical and imaging presentations may mimic brain tumour, cerebral abscess or other inflammatory disorders, and may necessitate a brain biopsy for diagnosis.

Case: A 65-year-old woman presented to our hospital with 10-day history of aphasia. She could not understand complex sentences. Magnetic resonance imaging demonstrated a 2x3x2 cm solitary large lesion associated mass effect and perilesional edema in left frontal lobe. This lobular shaped lesion was homogeneously enhanced by gadolinium on T1-weighted images. The patient underwent surgery for resection of the lesion. Postoperative pathology indicated chronic inflammation with reactive gliosis. 10 months later, she admitted to the hospital with right side weakness and progression of aphasia. Follow up magnetic resonance imaging demonstrated newly developed enhancing mass lesion in left deep gray matter. An open biopsy under navigation system was performed. Histological investigation was same as the previous result, chronic inflammation with reactive gliosis. The patient was treated with high-dose corticosteroid. The follow-up magnetic resonance imaging was improved dramatically after administration of steroid. No abnormal enhancing lesion is noted in the brain.

Conclusion: Distinguishing the tumefactive demyelinating lesions from neoplasm is important, since a misdiagnosis can lead to inadvertent brain irradiation or surgery. This case highlights the importance of considering tumefactive demyelinating lesions in the differential diagnosis of intracranial mass lesions. Timely diagnosis can save patient from potentially harmful aggressive treatment.

Poster Session 11
Case Report: Familial MS and NMO Cases

P-131
Familial neuromyelitis optica in mother and daughter with different Anti-aquaporin-4 antibody
Zhou Hongyu

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Background: Neuromyelitis optica is a distinct central nervous system demyelinating disease which Selective attack the optic nerves and spinal cord. It is associated
with the autoantibody NMO-IgG, which targets the water channel aquaporin-4. Neuromyelitis optica may be distinguished from typical multiple sclerosis on the basis of key clinical and neuroimaging characteristics in addition to detection of NMO-IgG. To our knowledge, there has not been a case between mother-daughter pair with different Anti-aquaporin-4 antibody. Several familial cases with the unified one(means AQP4 antibody positive)have been reported.

**Method:** To illustrate the clinical courses of NMO in a Aisa mother-daughter pair, which supports a hereditary predisposition to this disorder, as well as to discuss which factors could cause this different NMO-IgG test results within the same family.

**Participants:** Case report of a mother-daughter pair with NMO treated at the West China Hospital of Sichuan University.

**Results:** Using the latest diagnostic criteria both mother and daughter were diagnosed with NMO but with different Anti-aquaporin-4 antibody test results (the mother is negative while the daughter is positive).

**Conclusions:** Our familial cases show that genetically predisposition to this disorder, in addition to detection of NMO-IgG and anti-AQP-4 antibody, might not fulfill that requirement.

**P-132**

**Chinese sisters with NMOSD: one with AQP4 antibody seropositive and another with seronegative**

Wen Xu*, Wei Qiu*, Ying Chen*, Yongqiang Dai, Zhengqi Lu, Xueqiang Hu*

*equally contributed

MULTIPLE SCLEROSIS CENTER, DEPARTMENT OF NEUROLOGY, THE THIRD AFFILIATED HOSPITAL OF SUN YAT-SEN UNIVERSITY, GUANGZHOU, CHINA

**Background:** Neuromyelitis optica (NMO) was believed to arise from the factors such as genetics and environment. For Chinese, just one NMO family report before NMO-IgG were founded. In this case report, it is the first family report with NMO spectrum disorders (NMOSD) in Chinese after NMO-IgG were founded.

**Participants:** The demographic, clinical, neuroimaging, and anti-AQP-4 antibody status were investigated in these two sister patients. And the serum anti-AQP-4 antibody were also tested as seronegative in their two younger brother and a youngest sister.

**Observations:** The elder sister was 28 when she felt dizzy, poor eyesight and legs weakness in 2000, and were once diagnosed as multiple sclerosis. In 2011, her younger sister with 37 were diagnosed as NMO with AQP4 antibody seropositive, spinal cord lesion and were fulfilled with Wingerchuck criterion. We test the serum AQP4 antibody with the elder sister, and were found that the AQP4 antibody were seronegative. Meanwhile, the elder sister were diagnosed as NMOSD with reconsider.

**Conclusions:** This case may enhance the understanding of the genetic contribution to NMO and NMOSD. Our findings suggest that the familial history in patients with NMO or NMOSD can’t be ignored.

**P-133**

**Multiple Sclerosis And Neuromyelitis Optica In Sisters**

Zheng MM, Zhang XH

DEPARTMENT OF NEUROLOGY, BEIJING TIANTAN HOSPITAL, CAPITAL MEDICAL UNIVERSITY, BEIJING, CHINA

**Background:** Multiple sclerosis (MS) and neuromyelitis optica (NMO) are the most common inflammatory demyelinated diseases of central nervous system. Recently, NMO-IgG which targets the water channel aquaporin-4 was found, allowing sensitive and specific diagnosis of NMO. Some studies revealed that the two diseases are related to different genetic backgrounds and clinical manifestations.

**Objective:** The association and difference of MS and NMO are widely introduced, but NMO and MS in one family are rarely reported.

**Methods:** Here we reported two Chinese sisters with MS and NMO. The clinical manifestation and genetic analysis including human leukocyte antigen-DRB1 (HLA-DRB1), HLA-DRB3, interleukin-2 receptor gene (IL-2RA) and interleukin-7 receptor gene (IL-7RA) typing were described.

**Results:** The elder sister (Patient 1) was diagnosed as definite MS upon 2010 McDonald criteria. The younger sister (Patient 2) fulfilled the NMO revised criteria of Wingerchuck. The results of genetic analysis of the two patients are as follow.

<table>
<thead>
<tr>
<th>Genetic background</th>
<th>Patient1</th>
<th>Patient2</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-DRB1*1001</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>HLA-DRB3*0202</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>IL-2RA rs11256369</td>
<td>G43073C</td>
<td>G43073C</td>
</tr>
<tr>
<td>IL-7RA rs12358961</td>
<td>A43078T</td>
<td>A43078T</td>
</tr>
</tbody>
</table>

**Conclusions:** Two sisters have different manifestations corresponding to MS and NMO, but have nearly the same genetic background. Further studies are needed to explore the genetic linkage between the two diseases.
Case Report: NMO

P-134
Case Series of Neuromyelitis Optica
Report from Indonesia
Estiasari R, Sucipto, Samanta H, Komari N, Imran D

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Cipto Mangunkusumo Hospital Jakarta

Background: Neuromyelitis optica (NMO) is an uncommon disease in Indonesia but it affect productive age women and can cause sever disability. There is no report concerning the profile of Indonesian NMO cases until now. It is the first case series of NMO over the course of 12 month with anti aquaporin 4 result in Jakarta.

Objective: To report NMO cases in Jakarta.

Methods: Case series.

Results: We report 4 cases of NMO which all of the patients are women around 20-30 years old. From 4 cases only 1 case who had initial symptoms blurred vision. One case report the blurred vision after the diagnosis of myelitis. Two other patients did not report blurred vision but 1 of them had prolonged P100 latency of Visual Evoked Potential (VEP). All patients had paraparesis, hypesthesia and neuropathic pain. Spinal cord MRI showed LESCL in 2 cases, non LESCL in 1 case. Anti AQP4 antibody were detected in 1 case and negative in 2 cases. IgG of CMV was reactive in 2 cases. All patients had normal brain MRI. Three patients were treated with Methylprednisolone and 1 patients also received Azathioprine.

Conclusions: Myelitis in Indonesian NMO patients is more obvious than optic neuritis. Involvement of infection like CMV might play important role in the pathogenesis. AQP4 antibody test should be provided in Indonesia to help established the diagnosis of NMO

P-136
Chiasmal visual defect in a patient with neuromyelitis optica spectrum disorder
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Background & Significance: Neuromyelitis optica spectrum disorders (NMOSD) include definite NMO and limited forms of NMO with or without associated autoimmune systemic disorders. Chiasmal optic neuritis is a relative rare condition involving the optic chiasm, with a clinical appearance similar to that of retrobulbar neuritis. We report a case of a patient with NMOSD that developed a chiasmal visual field defect.

Case: A 35-year-old woman was admitted to our hospital after 4 days of visual field defect. Four months ago, she had a history of visual disturbance of both eyes, diagnosed as bilateral optic neuritis. Visual disturbance of both eyes were moderate improved after treatment with high dose methylprednisolone. In August 2011,
she presented visual field defect with mild decreased visual acuity. The examination revealed no abnormalities in eye movements and the pupils were isocoric and normally reactive to light. No relative afferent papillary defect was found. The pattern of visual field loss was a bitemporal hemianopia. Brain MRI revealed high signal intensities in intracranial segment of both optic nerves, optic chiasm and both optic tracts. The findings were felt consistent with the diagnosis of recurrent optic neuritis (chiasmal neuritis). Work-up for serological marker of demyelinating disease was negative, except anti-AQP4 antibody. She was treated with intravenous pulse of methylprednisolone 1.0 gram daily for 5 days. One week later, plasma exchange was performed because of poor response to steroid. After plasma exchange, visual symptoms were much improved.

Conclusions: We report NMOSD presenting optic chiasmal neuritis. The clinical similarity between chiasmal neuritis and optic neuritis suggests a shared pathophysiology, thus management of chiasmal neuritis follow the guidelines of the treatment of optic neuritis.

P-137
A Case of Recurrent Isolated Optic Neuritis of the Same Eye of 21 Years’ Duration with Positive Anti-Aquaporin-4 Antibody
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2Department of Medicine, Penang Medical College, Penang, Malaysia;
3Department of Neurology, Kuala Lumpur General Hospital, Kuala Lumpur, Malaysia.

Background: The discovery of anti-aquaporin-4 antibody (AQP4-Ab) has revolutionized our understanding of neuromyelitis optica (NMO), leading to correct diagnosis and treatment. It also broadens the clinical spectrum of this disease – the NMO spectrum disorder (NMOSD). We report a case of recurrent isolated unilateral optic neuritis (ON) of 21 years’ duration, recently being re-classified as NMOSD.

Case Report: A 43-year-old Chinese lady first developed left ON in 1991, at the age of 22 years. From 1991 to 2006, she had 8 episodes of ON of the same eye. During attacks, visual acuity was reduced to 6/60 or worse. She responded to intravenous methylprednisolone and tapering dose of oral prednisolone, with vision recovered to 6/18. Her right eye was never affected. Visual evoked potential showed prolonged P100 latency at left eye. Anti-nuclear antibody, lupus anticoagulant, anti-cardiolipin antibody, anti-Ro and anti-La were negative, with normal serial brain MRI. She never had symptoms or signs of myelitis. There was no episode of ON after 2006, despite not on medication. Her serum AQP4-Ab was recently tested positive and her diagnosis was revised to NMOSD.

Discussion: With the availability of AQP4-Ab testing, cases of ON of unknown aetiology, such as this lady, may turn out to be NMOSD. The longest reported duration of patient with ON who later developed myelitis, thus NMO, was 25 years. Our case is now 21 years from her 1st episode of ON, with recurrent episodes in the initial 15 years. In view of the possibility that she may develop into NMO later, azathioprine treatment was initiated.

P-138
Recurrent optic neuritis with negative aquaporin-4 antibody showing brain lesions on MRI
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Multiple Sclerosis Center, Department of Neurology, the Third Affiliated Hospital of Sun yat-sen University, Guangzhou, China.

Abstract: We report a Chinese case of recurrent optic neuritis (RON) with negative aquaporin-4 antibody (NMO-IgG) developed asymptomatic brain lesions on MRI. RON is a chronic inflammatory demyelinating disorder which may be associated with neuromyelitis optica (NMO) and multiple sclerosis (MS). After the discovery of NMO-IgG, the spectrum of disorders comprising standard NMO was expanded to NMO spectrum disorders (NMOSD). A few studies have shown that NMOSD had unique brain MRI features different from MS and other demyelinating diseases. Our case illustrates that RON with negative NMO-IgG may show similar clinical features, MRI characteristics, and therapy responsiveness to NMOSD with NMO-IgG.

P-139
A Case Of Spontaneous Pontine Hemorrhage Associated With Neuromyelitis Optica Spectrum Disorder
Park MS, Hah JS, Kim JH, Kim NY

Department of Neurology, Yeungnam University College of Medicine, Daegu, Korea

Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory demyelinating disease of the central nervous system and its pathophysiology is
neurological examination showed right central type dysarthria and left hemiparesis. NMO-IgG was seropositive. Cerebrospinal fluid examination showed negative results for oligoclonal IgG band. The IgG index was normal. Repeated brain MRI demonstrated new lesions on brainstem and cerebellum and left frontotemporal tumefactive lesion. Spinal cord MRI revealed longitudinally transverse myelitis (C3-5, T5-8). Therefore, the left frontotemporal tumefactive lesion biopsy was performed and finally led to the diagnosis of inflammatory demyelinating disease. Some lesions on MRI disappeared after two months of glucocorticoid, gamma globulin, and azathioprine treatment, but mild visual disorders and left hemiparesis remained as sequelae.

Conclusions: NMO may have tumefactive lesions. This is the first biopsy case of NMO with multiple tumefactive lesions.

P-140
A biopsy case of neuromyelitis optica with multiple tumefactive lesions
Bingjun Zhang, Wei Qiu, Zhengqi Lu

Multiple Sclerosis Centre, Department of Neurology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China

Background: Neuromyelitis optica (NMO) with multiple tumefactive lesions is reported rarely. Here, we report a case of NMO with multiple tumefactive lesions confirmed by biopsy.

Case: A 42-year-old male developed right arm weakness and facial paresthesia for 2 months. Brain MRI revealed multiple hyperintensities at similar areas. Symptoms were improved with steroid treatment, however some abnormal signal intensities were remained.

Five years later, he complained left side motor weakness and paraesthesia for 6 months. Brain MRI revealed multiple hyperintensities at left medial temporal lobe, corpus callosum, and periventricular white matter with gadolinium enhancement. After steroid therapy, symptoms were improved and follow-up MRI showed almost resolution.

Seven months later, sudden onset left extremities paresthesia was developed. Brain MRI and computed tomography revealed spontaneous ICH at right pons, corresponding to the previously demonstrated several demyelinating lesion. The AQP4-Ab was positive. We diagnosed NMO and the treatment was started with azathioprine and oral prednisolone.

Conclusion: Our patient developed ICH in corresponding to the location of previously demyelinating lesion. The association between demyelination and hemorrhage remains unclear. However, AQP4-Ab may compromise the integrity of the blood brain barrier and facilitate the perivascular inflammation and consequently lead to ICH. This indicates the possibility that ICH in NMO may be associated with AQP4-Ab vascular pathogenesis.

P-141
A Case Of Neuromyelitis Optica Spectrum Disorder Proven By A Brain Biopsy
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Byoung Joon Kim2

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2Department of Neurology, Samsung Medical Center, Gangnam-gu, Seoul, Korea

Background: Neuromyelitis optica spectrum disorder (NMOSD) is a heterogeneous group of central nervous system (CNS) autoimmune disorders associated with anti-aquaporin-4 antibody. Optic nerve and spinal cord are the main lesions and symptomatic cerebral lesions are possible. However initial hemispheric neurological symptoms and lesions may be misdiagnosed as a tumor. Here we report a case of NMOSD presented with a hemispheric lesion, which led to a brain biopsy.

Case report: A 47-year-old woman was admitted to the neurosurgery department because of headache, dysarthria, and lower extremity weakness which had developed 1 week prior to admission. On admission, the neurologic examination revealed right central type facial palsy and both leg weakness [Medical research council (MRC) grade 4]. The brain MRI showed tumorous lesions involving right frontotemporal and left medial temporal lobe, corpus callosum, and cerebral peduncle. She underwent a brain biopsy, which
showed leukocytoclastic vasculitis with eosinophils. Anti-aquaporin-4 was positive with 3+ intensity. Steroid and azathioprine achieved her clinical improvement and remission. But one year later she developed an episode of optic neuritis which was not responsive to IV steroid and plasma exchange.

**Conclusions:** NMOSD should be included in the differential diagnosis of patients first presenting with hemispheric neurological symptoms and tumorous cerebral lesions. Aquaporin-4 autoantibody test is essential for the diagnosis and establishing long-term treatment plan.

**P-142**

A Case Of Aquaporin 4 Antibody Positive And MRI Negative Progressive Myelopathy Responsive To Steroid Therapy

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¹Department of Neurology, Kyungpook National University Hospital, Daegu, Korea
²Department of Neurology, Samsung Changwon Hospital, Changwon, Korea

The MRI is becoming essential for diagnosis of spinal cord disease. But it is not uncommon in a patient clinically diagnosed myelopathy without any MRI abnormality. We report a 46-year-old patient presenting with progressive myelopathy with negative spinal cord MRI. Six months ago his both lower extremities weakness developed and slowly progressed. He felt his both legs were stiff and tingling. One month ago, he can't walk without cane. He visited our neurology department. He was social alcohol drinker and 20 pack-year current smoker. His past medical history was unremarkable. Sphincter dysfunction such as dysuria or constipation was absent. On neurological examination, his lower extremities muscle power was grade 4 around hip and knee joint and grade 3 around ankle joint. Deep tendon reflexes of both lower extremities showed hyperreflexia. Sensory level was present below fourth lumbar dermatome bilaterally. His gait was paraparetic and spastic. On whole spine MRI, although there were some degenerative change such as disc protrusion observed at cervical and lumbar spine, there was neither cord compression nor signal change. We performed the thorough evaluation for myelopathy such as cerebrospinal fluid study, serum autoimmune antibodies, paraneoplastic antibodies, immunoglobulin E, vitamin B12, serum and urine copper, aquaporin 4 antibody, and visual evoked potential, etc. The aquaporin 4 antibody result was positive. So we empirically treated him with methylprednisolone one gram per day for a week and then slowly tapered steroid with prednisolone. After steroid pulse therapy, his muscle power around ankle improved to grade 4 and his gait also improved. His clinical improvement continued and he can walk without any assistance two months later but leg spasticity persisted. Although there is wide differential diagnosis for a myelopathy with negative spinal MRI, the aquaporin 4 antibody may be beneficial to find a treatable disease such as neuromyelitis optica spectrum disorder. H.S. Song, H.-W. Lee, and J. H. Lee don’t have any conflict of interest with regards to the abstract/poster.

**P-143**

Mangalore model of epidemiological survey – A method for establishing minimum prevalence data for multiple sclerosis and allied disorders in resource poor countries.

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**Background:** In resource poor countries awareness of disease is poor, diagnostic facilities are limited and record keeping is poor. While community based neuro-epidemiological surveys in south India failed to identify demyelinating CNS disorders, a crude prevalence of <1/100,000 was reported for MS, based on hospital acquired data 3 decades ago.

**Objectives:** To determine prevalence and patterns of demyelinating CNS disorders in a well defined and stable population using secure sources, over a one year period.

**Method:** Mangalore, a city in the southwestern coast of India with an area 132.5 sq.km and a population of 419,306 was chosen. Selected specialists and allied health practitioners were sensitized. Registers for minimum patient data entry were placed in private clinics and teaching hospitals which covered the target population. Trained medical social workers collected data regularly. Identified patients were evaluated by L.P for confirmation and characterization of disease.

**Results:** In one survey year, 51 cases were identified. Prevalence rates calculated were MS- 4, NMO-0.9, ADEM-3.6, ATM 2.1 and ADEM 0.7/100,000.

**Conclusion:** MS is at least 4 times more prevalent in India than thought before and NMO is not over represented. This survey, besides establishing minimum prevalence data, heightened awareness about a hitherto less known disease locally and sets the background for larger surveys in India.
A Case Report and Review
YanPing,Guo1 Anthony,Traboulsee2

1Nanjing Brain Hospital Affiliated Of Nanjing Medical University; 2 MS Clinic of UBC Hospital , Department of Medicine ,Division Of Neurology, University of British Columbia,Canada

Case report: The patient is a 24-year-old woman originally from China 5 years ago with a prior history of mixed connective tissue disorder developed initial symptoms were abdominal pain with nausea and vomiting and general malaise. Two weeks later she developed double vision, during the next 72 to 96 hours she developed sequential severe bilateral optic neuritis (no light perception) and quadriplegia from complete transverse myelitis (EDSS score 9.0). An MRI of the cervical and thoracic spine showed a long extensive central cord lesion (holocord T2 hypersensitivity from medulla to coums which prominent involvement of the cervical and upper thoracic) and also as well as patchy areas of FLAIR hyperintensity within the brain in frontal, parietal and occipital lobes (FIGURE). Serology including positive ANA IF, positive rheumatoid factor, positive anti-Rho, mildly decreased TSH. Positive NMO antibody (serum and CSF). Lumbar puncture showing CSF with increased protein, increased immunoglobulins and positive for oligoclonal bands, mildly elevated white count at 14/mm3 and 92% lymphocytes. At the time of her admission, she had a five day course of IV Solu-medrol 1gram daily followed by Prednisone 50mg p.o. daily. Plasmapheresis was started concurrent with the steroid pulse for a total of 5 exchanges. There was no clinical improvement and at two weeks after the peak of her illness she received a single dose of IV mitoxantrone (12 mg/m2). The medication was well tolerated. Within two weeks post mitoxantrone, motor strength improved in all limbs from an MRC grade 0/5 (complete quadriplegia) to 4+/5 and vision improved to 20/25 with a residual central scotoma and return of normal bowel and bladder function (EDSS 2.5).

Department of Neurology, The Catholic University of College of Medicine

Background & Significance : Acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating disease of the central nervous system that generally develops after acute viral or bacterial infection or vaccination. ADEM is characterized by multiple foci of central nervous system damage, predominantly in the cerebral and cerebellar white matter, although basal ganglia and gray matter may also be involved. There are a few case reports associated with hepatitis B virus vaccination or infection Case : We reported a case of ADEM developed after vaccination for hepatitis B. Brain MRI showed high intensity lesion in the deep gray matter and cortex and spine MRI showed lesion preferentially corresponding to the gray matter in cervical and thoracic spinal cord. This pattern of the lesion was different from those in previously reported cases. We began to administer steroid hormone after admission. Patient rapidly recovered. Conclusions or Comments : We reported here an atypical case of ADEM associated with vaccination for Hepatitis B and MRI lesion.

Poster Session 13

Case Report: ADEM and MS Mimics

P-145
Preferential gray matter involvement in ADEM associated with vaccination of hepatitis B
Jae Young An, Kwang Soo Lee

Background & Significance : Acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating disease of the central nervous system that generally develops after acute viral or bacterial infection or vaccination. ADEM is characterized by multiple foci of central nervous system damage, predominantly in the cerebral and cerebellar white matter, although basal ganglia and gray matter may also be involved. There are a few case reports associated with hepatitis B virus vaccination or infection Case : We reported a case of ADEM developed after vaccination for hepatitis B. Brain MRI showed high intensity lesion in the deep gray matter and cortex and spine MRI showed lesion preferentially corresponding to the gray matter in cervical and thoracic spinal cord. This pattern of the lesion was different from those in previously reported cases. We began to administer steroid hormone after admission. Patient rapidly recovered. Conclusions or Comments : We reported here an atypical case of ADEM associated with vaccination for Hepatitis B and MRI lesion.

An adult patient with recurrent disseminated demyelinating encephalomyelitis presented as recurrent local soma numbness: a case report
Zhengqi Lu,Suqin Chen,Jian Bao,Bingjun Zhang, Xuejiao Men, Xueqiang Hu

Multiple Sclerosis Centre, Department of Neurology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China

Recurrent disseminated demyelinating encephalomyelitis(RDEM) is defined as the patient with acute disseminated demyelinating encephalomyelitis(ADEM) followed by a new event of ADEM with a recurrence of the initial symptoms and signs, 3 or more months after the first ADEM event, without involvement of new clinical areas by history, examination, or neuroimaging. Both of them are much more common in children and rarely seen in the adult. Herein we report a 27-year old female patient who complained about sudden onset of the numbness of left fingers and blur vision of both eyes after an acute diarrhea. Magnetic resonance image(MRI) of the cranial showed multifocal lesions in the right frontal lobe,bilateral corona radiata,bilateral temporal lobe, bilateral basal ganglia, and brain stem, with gadolinium enhancement. Lumber puncture showed that the
pressure of the cerebrospinal fluid (CSF) was normal, the white blood cells in the CSF were elevated slightly. The diagnosis of adult ADEM was made and large dose of Methylprednisolone intravenous injection made clinical recovery, though the MRI showed the lesions in the brain didn't vanish completely. She discharged without taking oral glucocorticoid. 10 months later she was suffered from the numbness of left tongue. The cranial MRI showed the lesions in the brain were enlarged on the basis of the old ones and enhanced with gadolinium. The diagnosis of RDEM was confirmed and she received another large dose of methylprednisolone therapy. She get good recovery and no new relapse in the following 2 years. This case illustrates that, adult ADEM patient has different clinical presentation from pediatric patient, encephalopathy may be absent in adult and mild syndrome does not always in accordance with the lesions in the brain. Though no pivotal studies has been made for the treatment of ADEM or RDEM, large dose of Methylprednisolone has reliable therapeutic effect in the acute recurrent phase which was accordance with the former reports about RDEM. The relapse rate of the RDEM seems much lower than other recurrent demyelinating disease, such as multiple sclerosis (MS) and neuromyelitis optica (NMO).

P-147
A case of multiphasic disseminated encephalomyelitis patient exacerbated by interferon beta treatment during 3-year follow up
Suqin Chen, Aimin Wu, Wei Qiu, Lei Zhang, Yinyao Lin, Zhengqi Lu
Multiple Sclerosis Centre, Department of Neurology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China

Objective: to describe a patient with total 5 attacks of demyelinating disease affecting the central nervous system (CNS) diagnosed as multiphasic disseminated encephalomyelitis (MDEM) exacerbated by interferon beta treatment.

Design: retrospective clinical case report.

Setting: institutional referral center for multiple sclerosis (MS).

Method: to collect the clinical characteristic and laboratory data and the magnetic resonance imaging (MRI) from the electronic medical record.

Result: The first attack presented as polysymptomatic and include encephalopathy, MRI showed multifocal lesions, predominantly involving white matter, the diagnosis of acute disseminated demyelinating encephalomyelitis was definite. The first relapse occurred 19 month later, whereas new longitudinal lesion in spinal cord, new patchy lesions in the posterior horn of the lateral ventricle, thalamus, mid-brain and cerebellum were found. Large dose of Methylprednisolone made a dramatic effect and long-term low-dose of oral Methylprednisolone was initiated for reducing relapse. She suffered the 2nd relapses 6 months from the 1st relapse despite taking the oral Methylprednisolone and the NMO-IgG was negative that the diagnosis of MS was taken into consideration and the treatment was shifted to interferon beta injection. 2 more relapses were observed in the following 8 months during the interferon beta treatment, both of the clinical and MR characteristic were worsen than the former 2 relapses and fulfilled the diagnosis criteria of MDEM raised by the International Pediatric MS Study Group in 2007. The diagnosis of MDEM was finally made and the interferon beta was stopped, no new relapse was observed in the following 12 months.

Conclusion: It is difficult to completely differentiate the CNS idiopathic inflammatory demyelinating disease including MDEM, MS and NMO on the basis of clinical course, lesion distribution on imaging, and laboratory findings. There are no diagnostic criteria for adult ADEM and MDEM. The diagnosis criteria for pediatric MDEM may be too strict and leading to over diagnosis of MS. Though large-dose of Methylprednisolone had dramatic effect in the acute relapse phase as it does in NMO and MS, long-term of low-dose Methylprednisolone may have no benefit of preventing relapse. Treating the MDEM patient with interferon beta may exacerbate the disease which is analogous with patient of NMO receiving interferon beta, which promoting that the MDEM may have the pathophysiologic mechanism more resemble with NMO rather than MS.

P-148
Adult-onset Leukodystrophy with Neuroaxonal Spheroids and Pigmented Glia Mimicking Primary Progressive Multiple Sclerosis
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Background: Adult-onset leukodystrophy with neuroaxonal spheroids and pigmented glia (ALSP) is a rare progressive white matter degenerative disease typically presenting with prominent neurobehavioural, cognitive and motor symptoms. Definitive diagnosis requires neuropathology demonstrating neuroaxonal spheroids and pigmented glia. Mutations in the colony stimulating factor 1 receptor (CSF1R) gene have been demonstrated in hereditary ALSP and de novo mutations in this gene may underlie sporadic cases.

Objective: We examine a case of ALSP and compare the clinical, radiological and pathological features with previous cases.

Methods: We reviewed the clinical findings, magnetic resonance imaging (MRI) and neuropathology of a case of ALSP mimicking primary progressive multiple sclerosis. We sequenced the coding sequence of exons 12-22 of the CSF1R gene, including splice junctions, to investigate the presence of an underlying genetic abnormality.

Results: A 42-year-old Caucasian male developed cognitive impairment and behavioural change over 14 months. MRI showed extensive periventricular and callosal T2 hyperintensities with associated alteration in diffusivity. Progressive neuropsychiatric disturbance and motor impairment led to severe disability. Evaluations for alternative diagnoses were negative. Brain biopsy demonstrated neuroaxonal spheroids, pigmented glia and demyelination in deep white matter. The neuropathological features were characteristic of ALSP. A novel CSF1R gene mutation was identified.

Conclusions: Whilst rare, ALSP should be considered in the differential diagnosis of primary progressive multiple sclerosis, particularly if there are prominent neurobehavioural features. Supportive MRI changes may heighten suspicion for ALSP, but definitive diagnosis requires brain biopsy. Future availability of clinical genetic testing may obviate the need for a tissue diagnosis.

P-149
Is It Metachromatic Leukodystrophy?
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Background: Metachromatic leukodystrophy (MLD) is a lysosomal storage disorder characterized by the deficiency of the enzyme arylsulfatase A, or of its activator protein saposin-B. MLD rarely has its clinical onset in young adults, with a combination of cognitive and behavioural symptoms and peripheral neuropathy.

Objective: Here we present an exceptional case with very late onset at 33 years of age and severe symmetric white matter hyperintensities in the periventricular area on T2-weighted images (Figure 1), without clinical or neurophysiological sign of peripheral neuropathy despite of slight recent impairment. Her great grandfather, grannie, mother, two of mother’s brothers and mother’s sister also had similar image manifestation(Figure 2). MLD was suspected and is it metachromatic leukodystrophy?

Methods: All eight exons and exon-intron boundaries of the arylsulfatase A gene (ARSA) and sphingolipid activator protein B gene (SAP-B) were amplified with polymerase chain reaction, which was followed by direct DNA sequencing. Levels of arylsulfatase A and galactocerebrosidase in the white blood cells were detected.

Results: The patient exhibited no mutation in any exon, and there was no loss of enzymatic activity.

Conclusions: The patient didn’t fulfill the diagnostic criteria of MLD, and maybe other genes and enzymatic activity associated to leukoencephalopathy should be detected to confirm the diagnosis.

P-150
A Case of primary Sjögren’s syndrome presented with hiccup and vertigo as initial manifestation
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Background & Significance: Sjögren’s syndrome (SS) can shows various neurologic symptoms as it involves the central, peripheral and autonomic nervous system. Neurological involvement occurs in 10-42% of the primary Sjögren’s syndrome (pSS). However, CNS involvement as an initial manifestation is rare. We report the case of pSS presented with vertigo, gait ataxia, and hiccup lasted about one month due to a discrete dorsal medullary lesion in primary SS.

Case: A 25-year-old woman developed dizziness and hiccup in the both arms 1 month before admission and aggravated her symptoms and suffered from vomiting and vertigo 2 days before admission. She had no medical history. On neurologic examinations she was revealed imbalance with gaze evoked nystagmus (GEN). Motor functions, sensation for pain and proprioception was normal. Brain MRI showed high signal intensity in the dorsal pons on the DWI, T2. At admission routine laboratory examinations of blood, and urine with anti-nuclear antibody, anti dsDNA Antibody and rheumatoid factor revealed no abnormal
findings. However, she had positive anti-SS-A/Ro Ab, anti SS-B/La Ab. Biopsy of salivary gland showed mild lymphoplasmacytic infiltration considered Sjogren's disease. Salivary scan revealed decreased activity of the both parotid glands and sublingual glands. The symptoms and lesions improved by the intravenous methylprednisolone therapy.

Conclusions: Previously, there are several cases about Sjögren's disease with involvement of central nervous system. But our case is unique because of hiccup and vertigo with dorsal medullary lesion as initial presentation in pSS. The horizontal GEN in this case may be caused by involvement of nucleus prepositus hypoglossi or medial vestibular nucleus as a horizontal neural integrator. Thus, this case suggests that pSS should be listed in the differential diagnosis of unknown origin brainstem lesion even without sicca symptoms.

P-151
Neurobrucellosis in a Patient with Multiple Sclerosis; a Case Report
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Introduction: Neurobrucellosis is an uncommon complication of brucellosis. Acute meningitis and encephalitis are the most common clinical manifestations, however symptoms may be protean and diagnosis requires a high index of suspicion in patients from endemic areas.

Case Presentation: Herein we report a 30 year old lady a known case of MS who came with ataxia and drowsiness, in physical examination and para clinical evaluations Neurobrucellosis was detected.

Discussion: Diagnosis is often based on neurological symptoms, serology, and suggestive brain imaging because cerebrospinal fluid culture yields are low. Multiple sclerosis (MS) is a chronic autoimmune disorder affecting the central nervous system (CNS) through demyelination and neurodegeneration.

P-152
Eales Disease with white matter lesions
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Abstract: Eales disease is an idiopathic, inflammatory, venoocclusive disorder of the peripheral retina resulting in retinal and vitreous hemorrhage. Eales disease is known to be the vasculitis restricted to the eye. Recently, the association of neurological conditions such as multiple sclerosis (MS), acute or subacute myelopathy, spastic paraparesis and stroke has also been reported. We report a 44-year-old male with Eales disease who had white matter abnormalities after 24 years of the signs of retinal periphlebitis.

P-153
Toxocara canis myelitis with the migration of lesion on follow up MR image
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Background: Toxocara canis is a common roundworm in dogs and other canids. Toxocara canis is an unusual cause of non-tumorous myelopathy. The migration of lesion may be pathognomonic for diagnosis of Toxocara canis myelitis. However there were few articles that demonstrated the migration of lesion on follow up image.

Case: A 52-year-old man was admitted to our hospital because of paresthesia in the lower limbs for 20 days. Examination confirmed dysesthesia in both lower limbs, up to T6 dermatome. Deep tendon reflexes were present and symmetric. Spinal magnetic resonance imaging (MRI) showed intramedullary T2-weighted hyperintensity from T3 to T6, with a contrast enhancement at level T5 along the posterior segment. CSF examination revealed 8 cells/μL with normal protein and glucose levels. CSF IgG index was 0.72 and CSF oligoconal band was negative. The patient improved only partially after receiving intravenous methylprednisolone 1 g for 5 consecutive days. One year after symptom onset, follow up MRI showed intramedullary T2-weighted hyperintensity from T4 to T5 with a focal enhancement in the left side at T5 level. Two years after symptom onset, follow up MRI revealed intramedullary T2-weighted hyperintensity from T4 to T5 with a focal enhancement in the right side at the same level. He had a history of ingestion uncooked cow liver. Antibody against Toxocara canis using the ELISA was positive in serum. A diagnosis of Toxocara canis myelitis was made. The patient was treated with albendazole 400 mg twice daily for 6 weeks.

Conclusion: I report a case of Toxocara canis myelitis
with the migration of lesion on follow up MR image.

P-154
Post Zoster Myelitis; Is this direct infection or post-infectious autoimmune disease?
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Background: Herpes zoster (HZ) is caused by reactivation of varicella zoster virus (VZV). Although HZ is not uncommon in general population, myelitis is a rare complication of VZV infection. The pathogenesis of myelitis associated with VZV remains controversy. We report 2 cases of post zoster myelitis which could be result from immune-mediated response.

Cases: Two patients admitted for acute weakness of right lower extremity with sensory disturbance under T4 and T9 level, respectively. Both of them had history of completely improved HZ with severe allodynia on right T6 dermatome approximately 2 months ago. ELISA for IgM antibodies to VZV in serum was negative and IgG was positive. Cerebrospinal fluid (CSF) analysis via lumbar puncture showed no pleocytosis and normal protein concentration without oligoclonal band. No VZV DNA was detected by PCR in CSF specimen. Spine MRI showed myelitis of thoracic spinal cord (T2-3 and T2-6 levels, respectively). The lesions were located in central with right-sided predominance on axial images. By high dose steroid and rehabilitation, the neurologic deficits were improved except mild paresthesia.

Conclusion: Previous reports of HZ myelitis suggested direct invasion of VZV and usually, spinal cord dysfunction began within 1 month of the onset of vesicular eruption. These 2 cases with longer interval between HZ infection and myelitis and no evidence of current VZV infection suggests that post zoster myelitis may be developed by post infectious autoimmune pathogenesis.

P-155
A Case Of Recurrent Unilateral Visual Loss Caused By Atypical Orbital Inflammatory Pseudotumor
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Background: An orbital inflammatory pseudotumor is a chronic inflammatory reaction, usually involving unilateral or bilateral orbital tissues. It typically presents with proptosis, oculomotor deficits, periorbital pain, lid swelling and ptosis. As an initial manifestation, visual deterioration caused by isolated optic nerve involvement by the idiopathic inflammatory process is rare and few reports are available now.

Case presentation: A 54-year-old woman presented with recurrent unilateral visual disturbance for three years. Visual acuity of right eye was decreased progressively. Initial ophthalmologic examination revealed no abnormal findings of right eye. Visual evoked potential study showed prolongation of P100 latency in right eye. Brain MRI displayed orbital inflammatory pseudotumor involving the right orbital apex and skull base. The patient was treated with oral corticosteroids and her clinical symptoms has improved.

DISCUSSIONS: This unusual manifestation resulted from the idiopathic orbital inflammatory pseudotumor involving the orbital apex is rare. Moreover, in the early clinical stage, an orbital inflammatory lesion may present itself only by visual disturbance. Therefore, it should be included in the differential diagnosis of isolated visual loss, though in the absence of initial orbital pain or external ophthalmoplegia.

P-156
Diffuse large B cell type Non Hodgkin lymphoma of pancreas in a patient with MS; a case report from Iran
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Introduction: Multiple sclerosis (MS) is a frequent chronic autoimmune demyelinating disease of the central nervous system (CNS). It was shown that multiple sclerosis (MS) was linked to reduced rates of cancer. herein we report a case of multiple sclerosis with Diffuse large B cell type Non Hodgkin lymphoma in head of pancreas, according to best of our knowledge this is the first case in this era.

Case Presentation: The patient is a 47 year old man a Known case of MS for 6 years. In a routine follow up
in outpatient clinic the patient had complain of a mild abdominal pain, and weight loss. Abdominal CT scan was performed for the patient which was in favour of lymphoma and fine needle aspiration (FNA) was recommended by the radiologist. FNA was done and according to the microscopic evaluations and immune histochemistry study, diffuse large B cell type Non Hodgkin lymphoma was diagnosed for him. **Discussion:** Recent epidemiological and immunological studies provide evidence for an association between Epstein-Barr virus infection and multiple sclerosis, suggesting a role of Epstein-Barr virus infection in disease induction and pathogenesis. Chronic suppression of cell-mediated immunity for treatment of MS may be associated with increased risk of malignancy in MS patients.

**P-157**

**Two Cases of Primary Central Nervous System Lymphoma; Radiologic Features Resembling Demyelinating Disease**

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**Background:** Primary central nervous system (CNS) lymphoma is a rare and aggressive brain tumor with unsatisfactory outcome. Here we presented two cases of PCNSL with neuroimaging and neuropathology.

**Case 1:** A 45 year-old woman present with bilateral visual disturbance. Initial brain MRI revealed small enhancing lesion in left midbrain and multifocal non-enhancing lesions involving bilateral fronto-temporo-parietal area and thalamus. The initial diagnosis was acute disseminated encephalomyelitis (ADEM). Even though she was treated with intravenous corticosteroid, visual disturbance did not improve. One month after symptom onset, severe headache and right side weakness developed. Follow up MRI showed multifocal enhancing lesions involving bilateral optic nerves, brain stem and white matter. A brain biopsy was performed and pathologic specimen revealed diffuse large B-cell lymphoma.

**Case 2:** A 62 year-old man presented with sudden onset of vertigo, tinnitus, and horizontal diplopia. Brain MRI revealed multifocal white matter lesions. The follow-up MRI two weeks after the initial imaging showed small enhancing lesion in corpus callosum. He was given a presumptive diagnosis of multiple sclerosis (MS). After oral corticosteroid therapy, clinical symptom slightly improved. However, symptom aggravated one month after therapy. The brain CT demonstrated multifocal hyperattenuated nodules. After a brain stereotactic biopsy, pathologic specimen revealed diffuse large B-cell lymphoma. He died due to gastrointestinal bleeding and septic shocked two months after diagnosis.

**Conclusion:** Primary CNS lymphoma can occasionally be indistinguishable from demyelinating diseases, such as ADEM or MS. Therefore, the possibility of lymphoma should be considered in the patients with tumefactive CNS demyelinating disease.