Epidemiology & Registry

P-1

Prevalence and prognosis in Canadian South Asians with MS (CSAMS Study)

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Objective: Multiple Sclerosis (MS) is less common in South Asian populations, previously reported prevalence rate of 0.2–1.3 per 100,000 of population in different parts of India with higher rates (24 per 100,000) in the mainly Parsi communities of Iranian descent in Mumbai and Pune. This suggests both environmental and genetic factors affect MS rates. Migration to countries with a high prevalence (Canada) may impact on the risk of having MS. We determined the prevalence and prognosis of MS in Canadian South Asians in British Columbia (UBC) MS Clinic database (COSTAR). Clinical course and Expanded Disability Status Score (EDSS) assessments were prospectively entered into COSTAR as part of routine clinical visits. Results: 73 patients were identified out of a cohort of 8781 MS patients. 77% were women. 32 were born in Canada. 84% had relapse onset MS, 15% primary progressive onset, 1 neuronomyelitis optica, and 1 Balô’s. The first clinical symptoms were optic neuritis in 21% and transverse myelitis in 44%. In all, 16/29 (53%) had oligoclonal bands in the cerebrospinal fluid. The estimated prevalence rate of MS is 36/100,000. In all, 14/73 (19.2%) patients reached EDSS 6 (FIGURE). Conclusion: MS is more common in Canadian South Asians than reported in Asian countries. The rates are approximately one-third that reported in the general Canadian population. The prognosis (time to EDSS 6) is similar to the general UBC MS population.

P-2

Sex ratio of multiple sclerosis: a study from Isfahan, Iran

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Background: Recent Studies have reported an increase in the female to male sex ratio of MS patients over a period of at least 30 years, based on the patients’ date of birth. Methods: This study was conducted on 1927 clinically definite Iranian MS patients of the province are now registered. The records of patients were reviewed, and the date of birth, gender, and related demographic and clinical data were extracted. Results: The female to male sex ratio by year of birth has been augmenting for the recent three decades and now is higher than 4:1. Conclusion: Also in Isfahan province of Iran, like other Western countries, MS is getting more common in women during the recent years. This has been associated with changes in the lifestyle and environment rather than genetic factors. However, this may be partially due to enhanced diagnosis by better diagnostic criteria, more advanced diagnostic tools, and higher awareness of physicians, in women who typically have milder forms of MS.

P-3

The global MSBase registry: facilitating collaborative research

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Background: Meaningful epidemiological outcome studies in MS require long-term observational data collection, substantially longer than the duration of clinical trials. Variation of relapse and disease progression rates require large, multi-centre datasets to attain sufficient statistical power to assess the real treatment effects. Variation of relapse and disease progression rates require large, multi-centre datasets to attain sufficient statistical power to assess the real treatment effects. Methods: We report our experiences operating and managing the first Web-based global MS outcomes data-basing system (http://www.msbase.org) over the last four years and highlight core issues, obstacles, and achievements. Results: The MSBase Registry currently has 51 active members from 25 countries that have contributed more than 8300 patient records. Eight substudies are in progress. More than 50% of patient records are updated every six months, and more than 90% at least annually. Conclusion: The MSBase registry is a simple and cost-effective method of accumulating large cohorts of outcomes data. It will facilitate the investigation of current and new treatment therapies and extend our understanding of the natural history of MS.

P-4

Temporal variation of onset of relapses in multiple sclerosis is not seasonal: results from the MSBase registry


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Background: Previous studies into time of onset of relapses have suggested that relapses are seasonal, with more relapses in spring and fewest in winter. The proposed mechanism is that reduced vitamin D levels at spring onset precipitate relapses. However, small numbers, differing diagnostic criteria, and the involvement of single regions limited these studies. Objective: To determine whether there is a temporal variation in onset of relapses using the MSBase registry, a large, additional text...
multi-centered cohort study of MS outcomes. Methods: Data was extracted on July 16, 2008. The dataset comprised 7860 cases with all forms of MS from 33 centers in 16 countries, including 25,784 documented relapses. Relapses with January 1 recorded as day of onset were excluded, leaving 22,684 in total including 5,542 first relapses. Relapses were stratified by hemisphere of residence and compared by season, quartile and month of onset. Statistical analysis was performed using chi-squared test. Results: 22,684 relapses (19,775 northern, 2,909 southern) were included. Relapses were significantly more common in spring in the northern hemisphere (P < 0.0001) and autumn in the southern hemisphere (P < 0.0001). June had the highest number of relapses than any other month in either hemisphere (P < 0.0001). These results were replicated with analysis of the 5542 first demyelinating event in MS cases (4801 northern, 741 southern).

Conclusions: A temporal variation in onset of relapses is present in both northern and southern hemispheres, however, this cannot be explained by season. This suggests that vitamin D levels have no effect on relapse onset.

P-5
Respiratory tract rather than cutaneous atopic allergies inversely associated with multiple sclerosis: a case-control study
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Background: It has been previously shown that genetic or environmental factors which promote susceptibility to allergic conditions protect against the development of Th1-mediated inflammatory disease of multiple sclerosis (MS). Purpose: To investigate the prediction value of lifetime atopic allergies in the development of the future MS, we designed a case-control study. Methods: Cases and controls were interviewed between December 2007 and April 2008 and were asked if they had had symptoms or diagnosis of atopic allergies. We categorized atopic allergies into two major groups of 1-respiratory tract allergy (RTA) including allergic rhinitis and asthma and 2-cutaneous allergy (CA) including urticaria, angioedema, and eczema. Results: Of 390 participants (193 controls and 195 cases), 125 healthy controls (64.1%) and 105 cases (53.8%) reported history of at least one type of atopic allergy (P = 0.04). Compared with those who had history of CA 47 cases (40.5%) vs 85 controls (43.6%); P = 0.54), participants who reported RTA (49 cases [25.1%] vs 85 controls [43.6%]; P < 0.001) seemed to have lower risk of the lifetime MS. Conclusions: There is a significant inverse association between RTA and MS that is compatible with a Th1/Th2 imbalance. History of RTA could be considered clinically useful risk-reducing factor of MS.

Genetics
P-6
Genetic susceptibility of HLA DRB1 to multiple sclerosis and oligoclonal bands in Australians
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Multiple sclerosis (MS) is a disease with immune mediated features associated with the human leukocyte antigens (HLA) complex, in particular, the HLA-DRB1*1501 allele (HLA-DR2), which is present in 56-65% of MS versus 24-28% of controls in Caucasian populations. The HLA-DRB1*1501 has been associated with positive oligoclonal bands (OCB) in some reports. The aims of this study were to study the HLA-DRB1 genotype profile in an Australian MS cohort. Blood samples were collected from our well-characterized cohort of 975 Western Australian patients with demyelinating disease who were willing to participate in this study. A control group of 189 Caucasian individuals, from a rural Western Australian community was used for comparison. Our preliminary results showed high frequencies of DRB1*1501 allele carried in conventional MS (52.9%, 118/223), primary progressive MS (55.6%, 10/18), and optic-spinal MS (57.1%, 8/14) patients, which are significant compared with frequencies in the control group (41.3%, P < 0.001). The presence of DRB1*1501 was significantly associated with positive OCB (P = 0.015). Our findings confirmed the important role of immunogenetics in MS pathogenesis.

Cytotoxic T lymphocyte associated antigen-4 (CTLA-4) exon 1 A/G polymorphism in Iranian patients with multiple sclerosis
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Background: Cytotoxic T lymphocyte antigen-4 (CTLA-4) is a T-cell surface receptor of activated T cells. Material and Methods: We studied 100 Iranian patients with clinically definite multiple sclerosis (MS) and 100 ethnic, sex- and age-matched controls. CTLA-4 exon 1 A/G polymorphism was compared in patients and in controls. Results: There was no statistically significant difference in the allele (OR: 1.19, CI 95%: 0.76–1.85, P = 0.4) and genotypes (OR: 1.60, CI 95%: 0.911–2.824, P = 0.102) distribution among patients and controls. Also gender, course, and progression index did not show any statistically significant differences in allele and genotype distribution of A/G polymorphism. Conclusion: As a non-European patient population, our results are consistent with the major previous studies showing no significant associations between CTLA4 exon 1 polymorphism and neither MS nor any of its subtypes.

Clinical symptomatology & course
P-8
Color vision deficiency in multiple sclerosis with and without history of optic neuritis
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Background: Using Ishihara color vision test, we considered color vision deficiency (CVD) as an indicator of optic neuritis (ON) and accordingly explored asymptomatic ON among multiple sclerosis (MS) patients. Materials & Methods: An observational study was carried out on a series of 110 consecutive MS patients from April to July 2007. Participants with documented congenital CVD or eyes with total blindness were excluded. Using Ishihara color vision test, we considered color vision deficiency (CVD) as an indicator of optic neuritis (ON) and accordingly explored asymptomatic ON among multiple sclerosis (MS) patients. Results: Among 214 included eyes, Ishihara color vision test results were normal in 162 (75.7%) and 52 (24.3%) were shown to suffer from various levels of color blindness. Of 85 eyes with no history of ON, related symptoms that were suggestive for undiagnosed ON, or concurrent ON at the time of the study were considered asymptomatic ON patients. Results: Among 214 included eyes, Ishihara color vision test results were normal in 162 (75.7%) and 52 (24.3%) were shown to suffer from various levels of color blindness. Of 85 eyes with no history of previous or existing ON, eight (9.4%) has been reported to have CVD. Conclusion: CVD is prevalent among MS patients and can be an indicator of asymptomatic ON/MS. Ishihara color vision test is an easy to use instrument that might help MS patients to detect and follow their CVD and physicians to diagnose and treat the in-progress and subclinical ON/MS.

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Patterns of visual field defect in CNS demyelinating diseases

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Background: The common pattern of visual field defect (VFD) in acute optic neuritis (ON) or multiple sclerosis (MS) is known to be central field defect. In case of peripheral VFD, other causes of demyelinating diseases, such as neuromyelitis optica (NMO) or vasculitis, should be considered. The exact patterns of VFD, however, have not been clearly defined. Objective: To investigate the patterns of VFD in CNS demyelinating diseases. Methods: 42 patients (12 men and 30 women) between 1996 and 2008 with clinically defined ON, MS, NMO, or vasculitis were reviewed retrospectively. They received ophthalmologic evaluation using manual Goldmann perimetry. The patterns of VFDs were classified into 11 types by an ophthalmologist according to the location of field defect and grossly divided into two groups; central defects such as central scotoma and peripheral defects such as wedge-shaped or hemianopic defects. We compared VFDs between 1) ON, 2) MS with short cord lesion (SCL), 3) with long cord lesion (LCL) extending over three vertebral segments, 4) MS without cord lesion, and 5) vasculitis. Results: The patients with ON tended to have more central defects (central: 14, peripheral: 4). The patients with long cord lesion had relatively more peripheral defects (central: 4, peripheral: 3) compared to other MS groups. No patients with short cord lesion (6 patients) or without cord lesion (4 patients) had peripheral defects. In the cases with Sjogren disease (4 patients), all had peripheral field defects. Conclusions: This study demonstrated that the patients with classical MS had central VFDs. Patients with NMO showing long cord lesion or Sjogren disease were more likely associated with peripheral VFDs.

Cognitive function in patients with clinically isolated syndrome suggestive of multiple sclerosis in Thailand – data from CogniCIS, a worldwide longitudinal study

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Background: The common pattern of visual field defect in acute optic neuritis (ON) or multiple sclerosis (MS) is known to be central field defect. In case of peripheral VFD, other causes of demyelinating diseases, such as neuromyelitis optica (NMO) or vasculitis, should be considered. The exact patterns of VFD, however, have not been clearly defined. Objective: To investigate the patterns of VFD in CNS demyelinating diseases. Methods: 42 patients (12 men and 30 women) between 1996 and 2008 with clinically defined ON, MS, NMO, or vasculitis were reviewed retrospectively. They received ophthalmologic evaluation using manual Goldmann perimetry. The patterns of VFDs were classified into 11 types by an ophthalmologist according to the location of field defect and grossly divided into two groups; central defects such as central scotoma and peripheral defects such as wedge-shaped or hemianopic defects. We compared VFDs between 1) ON, 2) MS with short cord lesion (SCL), 3) with long cord lesion (LCL) extending over three vertebral segments, 4) MS without cord lesion, and 5) vasculitis. Results: The patients with ON tended to have more central defects (central: 14, peripheral: 4). The patients with long cord lesion had relatively more peripheral defects (central: 4, peripheral: 3) compared to other MS groups. No patients with short cord lesion (6 patients) or without cord lesion (4 patients) had peripheral defects. In the cases with Sjogren disease (4 patients), all had peripheral field defects. Conclusions: This study demonstrated that the patients with classical MS had central VFDs. Patients with NMO showing long cord lesion or Sjogren disease were more likely associated with peripheral VFDs.

Cognitive function in patients with early multiple sclerosis in Asia: data from CogniMS, a worldwide longitudinal study

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Objective: To measure cognition, fatigue, depression and health-related quality of life (HRQoL), and the interrelation of these parameters in patients with early MS in Asia. Background: Longitudinal data on cognition in early MS patients is rarely documented. The CogniMS observational study collects longitudinal data from a large patient cohort worldwide. This is the first report on the neuropsychological characteristics of patients with early MS from Asia. Methods: Patients with early MS (diagnosed within two years) treated with IFNB-1b were assessed every six months over two years. Cognitive function was assessed by the PASAT and the FST. Fatigue was assessed by the Fatigue Severity Scale (FSS), depression by the Center for Epidemiologic Studies Depression Scale (CES-D), HRQoL by the EQ-5D. Results: Recruitment has ended and baseline data are shown from 111 patients from Asia (South Korea 67; Taiwan 23; Thailand 21). Median age was 35.0 years and 70.0% of patients were women. Median time since onset of MS symptoms was 14.23 months, median Expanded Disability Status Score was 2.0. The median PASAT score was 48.0 and 19.2% of patients were likely impaired. The median FSS total score was 4.05. In 55.0% of patients, FSS scores were suggestive of fatigue and 25.0% of CES-D scores indicative of depression. The median EQ-5D index score and the EQ-5D VAS were 0.69 and 70.0, respectively. Conclusions: Unique observational data relating to cognition, fatigue, depression and HRQoL, in Asian patients with early MS treated with IFNB-1b will be presented. The longitudinal data of these patients will elucidate the pattern in cognitive and emotional variables over time. Further refinements and data collection are necessary to validate current scales. Study supported by: Bayer Schering Pharma AG, Berlin, Germany

Clinical and demographic characteristics of multiple sclerosis with late onset

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Background: While multiple sclerosis (MS) is generally regarded as a neurologic disease of younger adults, some patients manifest the first symptoms of MS after the age of 50; a form of MS known as late-onset multiple sclerosis (MS-LON). This study is the first to report on the characteristics of patients with late-onset MS in Asia. Methods: We conducted a cross-sectional study to describe clinical and demographic characteristics of patients with late-onset MS in Asia. Results: We recruited 43 patients with late-onset MS. The median age at onset was 54.0 years and 80.0% of patients were women. The median Expanded Disability Status Score was 2.0. The median PASAT score was 48.0 and 19.2% of patients were likely impaired. The median FSS total score was 4.05. In 55.0% of patients, FSS scores were suggestive of fatigue and 25.0% of CES-D scores indicative of depression. The median EQ-5D index score and the EQ-5D VAS were 0.69 and 70.0, respectively. Conclusions: Unique observational data relating to cognition, fatigue, depression and HRQoL, in Asian patients with early MS treated with IFNB-1b will be presented. The longitudinal data of these patients will elucidate the pattern in cognitive and emotional variables over time. Further refinements and data collection are necessary to validate current scales. Study supported by: Bayer Schering Pharma AG, Berlin, Germany

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MS (LOMS). **Objectives:** This study was designed to highlight the clinical and demographic features of patients with LOMS in Isfahan, Iran. **Methods:** The clinical records of LOMS patients who were followed at Isfahan MS Society (IMSS) were gathered. IMSS database consists of nearly all MS patients in the province. **Results:** Among 2247 MS patients (1751 women, 496 men) registered in IMSS from April 2003 to January 2008, 32 (1.42%) were diagnosed with LOMS. The mean age at onset was 54.7 ± 1.8. The female to male ratio was 1.3:1. The relapsing-remitting course was the predominant disease course among the patients (75%). The most common initial presentation was brainstem symptoms (34.4%); other symptoms included sensory disturbances (28.1%), optic neuritis (25%), and motor deficits (25%). The mean Expanded Disability Status Score and Progression Index were 2.3 ± 1.5 and 0.66 ± 0.3, respectively. **Conclusion:** Compared to other populations with high prevalence of MS, we observed a lower percentage of MS patients with LOMS. The disease progressed with equal pace in men and women and the risk was almost equal for both sexes. LOMS patients compared to other MS patients had a faster disease progression, higher rate of primary progressive, more conversion to secondary progressive course, experience fewer sensory symptoms and optic neuritis, but more brainstem symptoms as initial symptom.

**P.13**

The Multiple Sclerosis Severity Score (MSSS) re-examined: EDSS rank stability in the MSBase dataset increases 5 years after onset of multiple sclerosis


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**Background:** The Multiple Sclerosis Severity Score (MSSS) is an Expanded Disability Status Score (EDSS)-based severity rank for a given disease duration. It has been validated for use comparing disease progression among the patients (75%). The most common initial presentation was brainstem symptoms (34.4%); other symptoms included sensory disturbances (28.1%), optic neuritis (25%), and motor deficits (25%). The mean Expanded Disability Status Score and Progression Index were 2.3 ± 1.5 and 0.66 ± 0.3, respectively. **Conclusion:** Compared to other populations with high prevalence of MS, we observed a lower percentage of MS patients with LOMS. The disease progressed with equal pace in men and women and the risk was almost equal for both sexes. LOMS patients compared to other MS patients had a faster disease progression, higher rate of primary progressive, more conversion to secondary progressive course, experience fewer sensory symptoms and optic neuritis, but more brainstem symptoms as initial symptom.

**P.16**

Objectives: To assess the association of the MSSS with disease duration in a large multi-centre cohort study.

**Methods:** The multiple sclerosis (MS) cohort was comprised of all MS patients in the province. **Results:** Among 2247 MS patients (1751 women, 496 men) registered in IMSS from April 2003 to January 2008, 32 (1.42%) were diagnosed with LOMS. The mean age at onset was 54.7 ± 1.8. The female to male ratio was 1.3:1. The relapsing-remitting course was the predominant disease course among the patients (75%). The most common initial presentation was brainstem symptoms (34.4%); other symptoms included sensory disturbances (28.1%), optic neuritis (25%), and motor deficits (25%). The mean Expanded Disability Status Score and Progression Index were 2.3 ± 1.5 and 0.66 ± 0.3, respectively. **Conclusion:** Compared to other populations with high prevalence of MS, we observed a lower percentage of MS patients with LOMS. The disease progressed with equal pace in men and women and the risk was almost equal for both sexes. LOMS patients compared to other MS patients had a faster disease progression, higher rate of primary progressive, more conversion to secondary progressive course, experience fewer sensory symptoms and optic neuritis, but more brainstem symptoms as initial symptom.

**P.14**

Spectrum of presentation of patients with multiple sclerosis in Malaysia: results of a multicenter study from the Ministry of Health in Malaysia


**Hospitals within the Ministry of Health of Malaysia**

**Objectives:** The main objective was to look at patient demographics, epidemiology, clinical features, neuroimaging, access to treatment, and current functional status with or without treatment in patients presenting with classical Western type Multiple Sclerosis and Asian type optico-spinal MS. **Methodology:** A multicenter retrospective observational study based on patients presenting to government hospitals within the Ministry of Health in Malaysia over a 10-year period from 1998 to 2008. A questionnaire was distributed to government hospitals throughout Malaysia. A total of 100 patients were included in this study. **Results:** Most patients were young, females, majority Malay and Chinese presenting with classical Western type multiple sclerosis and optico-spinal type variants. Major MS, relapses and non-relapse fluctuations on EDSS. MSSS at 5 years from diagnosis is highly predictive of MSSS at 10 years and may have prognostic value in individuals.

**P.15**

Natural history of recurrent optic neuritis: 5-year follow-up results

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**Background:** Recurrence in optic neuritis (ON) is uncommon clinical phenomenon and there are only few studies about clinical course and characteristics about recurrent ON. Recurrent ON may occur in isolation or as a part of initial clinical manifestation of MS or neuromyelitis optica (NMO). In previous Western study, five-year conversion rate to NMO was 12.5% and MS was 14.4%, respectively. In this study, we investigated the natural history in patients with recurrent ON in Asians. **Methods:** We performed a prospective cohort study of patients with optic neuritis. Sixty-two patients with optic neuritis were enrolled, and 17 of them had a recurrent ON. Excluded were those who showed any evidence of multiple sclerosis at initial assessment, and those with prior demyelinating attacks. The patients were followed for the occurrence of optic neuritis or conversion to MS and NMO for five years. **Results:** The mean follow-up period of 58 months, yielding a five-year cumulative rate of MS or NMO of 23.5% (n = 4). The consecutive relapsing sites were spinal cord (n = 3) supporting NMO or optico-spinal MS, and brainstem and cerebellar hemisphere (n = 1) suggesting MS. **Discussion:** In this study, although the enrolled number of patient was small, the result suggests that the natural
history of recurrent ON does not differ between Asian and Western populations. Most patients with recurrent ON should be monitored in suspicion about conversion to MS or NMO. Although pathogenesis of isolated recurrent ON is not yet revealed, difference mechanism between isolated recurrent ON group with conversion group is suspected.

Imaging

P-16
Correlation between plaque characteristics (ROI) in MRI and severity and duration of multiple sclerosis
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Introduction: Multiple sclerosis (MS) is the most common disease caused by an inflammatory demyelinating process in the CNS, which features a relapsing and remitting course with disseminated lesions in white matter. The diagnosis of MS is usually established by a combination of history, physical examination, laboratory tests, and imaging findings. MRI is a highly sensitive tool forms, with 95% patients with clinically definite MS demonstrating brain abnormalities. Expanded Disability Status Score (EDSS) is a number between 0 and 10, which is determined by neurologist to express the severity of disability. Several Disability Status Score (EDSS) is a number between 0 and 10, which is determined by neurologist to express the severity of disability.

Material and Methods: 40 clinically definite MS patients were evaluated and MR images were obtained in the MRI unit of Radiology Department. Precontrast images include axial and sagittal T1, axial and coronal T2-weighted images, sagittal proton density, and axial flair. Contrast-enhanced images were taken in five minutes. Number of plaques, diameter, and the site of the largest plaque and the area of brain containing most of the lesions in flair and T2W sequences, and also presence of enhancing plaque in PC-T1W images were determined. Then MR numbers (ROI) of the largest plaque as well as the enhancing one (if any) were determined in all sequences. Results: Mean age of the patients was 28.3 ± 9.1 years. Only 9 of 40 patients had enhancing plaque (22.5%). The mean diameter of the largest plaque was 10.20 ± 4.2 mm. In 35 of 40 patients, the largest lesion was in periventricular deep white matter (87.5%). In 29 patients (72.5%), the plaques were gathered in periventricular DWM, in six patients (15%) in centrum semiovale, in two cases (5%) in juxtacortical area, and in three cases (7.5%) were diffusely distributed. The EDSS of our patients which was defined by neurologist consulted is between 0 and 6.5 (mean = 1.66). We defined ROI of plaque, as well as adjacent white and gray matters. Mean ROI of MS plaque in T1 = 611, in T2 = 1312, FLAIR = 1131, proton density = 1354. In evaluating the correlation between age, duration with EDSS, P value is 0.426 and 0.696, respectively. The P values of correlations between size of largest, number of plaques, and presence of enhancing lesion and EDSS are 0.779, 0.580 and 0.729 respectively. Also in analyzing the correlations between ROI of plaques, adjacent white and gray matter and EDSS, none of the P values are less than 0.05. Discussion: As studied in the results, none of P values in the correlation of multiple factors and EDSS are 0.05 or less. So we can conclude that EDSS is not affected by age, duration, and plaque characteristics such as ROI, EDSS is not in correlation with ratio of ROIs of plaque to white matter neither. But a significant negative correlation (\( P = 0.027 \)) between ROI of plaque in FLAIR sequence and duration of disease is detected in our study which states that in old MS cases ROI of plaques in FLAIR decreases. Similar relation is not seen in other sequences. Also a correlation between number of plaques and diameter of the largest one is noted (\( P = 0.05 \)).

P-17
Unusual MRI findings in Canadians Asians with MS (CAMS Study)
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Objective: MRI abnormalities in MS in general can be quite heterogeneous. In Asians with MS, longitudinally extensive cord lesions (LESCL; ≥ 3 segments) have been reported which are not typically seen in Caucasians with MS. Other atypical lesions, though not restricted to Asians, include long corpus callosum lesions, long brain stem lesions, and large brain lesions (>2 cm in diameter). Our goal was to determine the frequency of unusual lesions in Asian-Canadians with MS. Methods: Asian patients with clinically definite MS and are registered at the UBC MS clinic were eligible. Those with available MRI scans of the brain and/or spinal cord were included. MRIs were reviewed by an experienced radiologist (DL) blinded to clinical history and disease phenotype. Results: 135 MRIs from 41 consecutive patients were reviewed (Table). For conventional MS (CMS) (N = 82) and OMS (N = 15): 0% and 27% had normal brain MRI; 29% and 33% had LESC, 27% of both groups had atypical brain lesions (FIGURE). Conclusion: Unusual MRI features are common in Canadian Asians with MS and similar to reports from Asia. The longitudinally extensive spinal cord lesions were the commonest abnormality detected with a similar occurrence in CMS and OMS. Radiologic features alone may not be able to distinguish CMS from OMS. Alternatively, Asian MS patients with unusual MRI features could represent a distinct pathologic subgroup of MS patients such as NMO despite overlapping clinical presentations.

P-18
Clinical features of patients with longitudinally extensive spinal cord lesions in WA
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Introduction: Longitudinally extensive spinal cord lesions (LESCL, ≥ 3 segments in sagittal MRI of spinal cord) are not specific for neuromyelitis optica (NMO) or OSMS in Oriental populations. The prevalence of LESC in Western MS patients has been reported to occur in 10–36% of cases. Therefore, we examined the clinical, MRI, and laboratory features of Caucasian patients with LESC in Western Australia. Methods: Retrospective analysis of patients with LESC in our MS cohort. Results: 22 Caucasian patients with LESC were identified. Biopsy or autopsy was performed in five patients. Two patients had monophasic disease (AM), the remaining relapsing patients would be classified as conventional MS (CMS) in 12 (54.5%), NMO spectrum in eight (36.4%), including four recurrent NMO, four recurrent AM (RAM). The mean length of follow-up was 11.9 years (max 32 years), with 12 patients (54.5%) >10 years, eight (36.4%) >15 years, and 5 (22.7%) >20 years. Three patients (13.6%) were followed up from onset to death. Three patients (13.6%) had a benign course (Expanded Disability Status Score [EDSS] <3.0) after >10 years onset of LESC. The mean length of LESC was 6.3 segments (3–19). Diencephalic lesions on MRI were found in one patient who was diagnosed with CMS. Three patients with phenotypical NMO showed negative cerebral images at onset, but developed demyelinating brain lesion characteristic of classic MS later. One RAM patient with the longest LESC at onset in our group (C1-T12) showed a completely normal spinal cord MRI appearance after 11 years follow-up, 11 patients had cerebrospinal fluid examination, and OCB was positive in three (27.2%). Aquaporin-4 (AQP4)-IgG was tested in nine patients (7 NMO spectrum, 2 CMS) with only one (11%) positive in rAAM.
Conclusions: The patients with LESCL had highly heterogeneous clinical characters. Our preliminary data showed that LESCL are not infrequent in typical Western CMS; LESCL patients may have a benign clinical course; diencephalic lesions may happen in otherwise typical CMS with LESCL; NMO patients with LESCL may evolve into CMS with typical cerebral lesions; OCB positive rate was low. AQP4-IgG and NMO-IgG were rarely found in this predominantly Anglo-Celtic cohort despite the presence of LESCL, suggesting much lower sensitivity than in other published cohorts. This may be due to immunogenetic factors as reports from other group have a high population of non-Caucasian patients.

Brain magnetic resonance image findings in neuromyelitis optica IgG positive patients
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Background: Neuromyelitis optica (NMO)-IgG was included as one of the three supportive diagnostic criteria for NMO with good sensitivity and specificity. However, previous studies were focused on the findings of spinal cord MRI and positive rate of NMO-IgG for NMO. Our hospital is large, tertiary referral center in Korea and paraneoplastic antibodies including NMO-IgG have been investigated since 2006.

Objective: To investigate the NMO-IgG positive patients and describe their clinical characteristics and Brain MRI findings.

Patients and Method: We evaluated 958 patients who were tested for paraneoplastic antibodies with NMO-IgG, using the indirect immunofluorescent method in Asan Medical Center between January 2006 and August 2008, retrospectively.

Results: Among the patients (n = 18) whom NMO-IgG was detected, 10 patients had episodes of both optic neuritis and acute myelitis. Two patients had multiple sclerosis including recurrent myelitis without the history of optic neuritis and one patient experienced the only one episode of myelitis. The mean age at onset (n = 13, female 84.6%, mean NMO titer, 1:420) was 31.0 ± 14.0 years. The mean clinical attacks of optic neuritis and acute myelitis were 2.0 ± 1.8 and 3.5 ± 2.4 during the follow-up period (mean 59.8 ± 42.1 months), respectively. Among the 12 of 13 patients underwent brain MRI, four patients showed no abnormality. The frequent brain lesions (n = 8, symptomatic: 5 and asymptomatic: 3) were juxtacortical (five patients), subcortical areas (five patients), corpus callosum (six patients), periventricular white matter abut to lateral ventricle (six patients), lesions adjacent fourth ventricle including middle cerebellar peduncle (five patients).

Conclusions: Symptomatic brain lesions were common in NMO-IgG positive patient as much as asymptomatic lesion.

Clinical and MRI Characteristics of CNS Aquaporin-4 Autoimmunity
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Objectives: To evaluate the clinical and MRI characteristics of neuromyelitis optica (NMO) spectrum disorders with anti-aquaporin-4 (AQP4) antibody seropositivity Methods: We retrospectively analyzed the demographic, clinical, and MRI findings of patients with anti-AQP4 antibody confirmed by indirect immunofluorescence staining. Totally, 45 consecutive patients were included. All patients were diagnosed as having one of NMO spectrum disorders. Results: There was a female predominance (M:F = 5:40) with mean onset age of 29.9 ± 10.8 years (range 10.8–52.2 years). Optic neuritis (ON) (20 patients, 44.4%) and myelitis (19 patients, 42.2%) were the most common presenting symptoms, however, six patients (13.3%) presented with brain symptoms. Over the 5.7 ± 4.5 years of average disease duration, ON occurred in 32 (71.1%) patients, myelitis in 44 (97.8%) patients, and symptomatic brain involvement in 20 (42.2%) patients. The mean annualized relapse rate was 2.7 ± 2.2. Most patients had severe relapses in their clinical courses; approximately 81% of the patients with ON had visual acuity less than 0.1 in at least one eye and 74% of patients with myelitis were unable to ambulate without assistance. In the cerebrospinal fluid study, oligoclonal bands were present in three patients (6.7%) and IgG index was elevated in 12 (26.7%) patients. On cord MRI, a contiguous cord lesion extending over three vertebral segments was found in all patients with myelitis except one. Almost all cord lesions (94.7%) preferentially affected the central gray matter with cord swelling. On follow-up MRI, cord atrophy was common (57.1%). On brain MRI, 39 patients (87.7%) had brain lesions in their disease course and 20 patients (44.4%) had symptomatic brain lesions. Six patients (13.3%) had brain symptoms at the first presentation. The abnormalities of brain MRI were classified into five categories: (1) lesions involving corticospinal tracts (e.g., posterior limb of internal capsule, cerebral peduncle) (21 patients, 46.7%); (2) extensive hemispheric lesions (14 patients, 31.1%); (3) periependymal lesions surrounding lateral ventricles (19 patient, 42.2%); (4) periependymal lesions surrounding third & fourth ventricles (12 patients, 26.7%); (5) medullary involvement as an extension of a cervical myelitis (17 patients, 37.8%). Sixty-one percent of the patients showed at least two characteristic abnormalities among five categories.

Conclusions: Our results suggest that the clinical and MRI features of patients with anti-AQP4 autoantibody are distinct from multiple sclerosis: (1) clinical attacks are frequent and severe; (2) brain involvements are common as previously appreciated and often characteristic enough to differentiate from prototypic MS.

Pathomechanism & experimental study

The study of serum free testosterone in women with multiple sclerosis comparing with healthy women
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Objective: In this study, concentration of serum free testosterone was measured in women with MS and healthy women and the result was compared for evaluation of role of free testosterone in both mentioned groups as well the relationship with EDSS, duration of disease, type of disease, and GAD enhancement in brain MRI.

Patients (Materials) and Methods: In our study, the patients group was 35 cases and the healthy women group was 25.

Results: Patients in MS group had the following characteristics: men age: 32, mean duration: six years, Mean EDSS: 3.6. Disease type: (RR: 24, secondary progressive: 8, primary progressive: 2, relapsing progressive: 1), GAD enhancement in MRI: nine patients. In this study, concentration of serum free testosterone was considerably lower in women with MS compared with healthy women (P < 0.03 ). As well the more duration of disease the less serum free testosterone and there was no relationship between free testosterone and EDSS, type of disease and GAD enhancement in brain MRI. Conclusion: we concluded that serum free testosterone can have a protective role in women with multiple sclerosis.
Evaluation of serum and cerebrospinal fluid magnesium and zinc concentration in patients with multiple sclerosis: a case-control study
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Background: Environmental factors are found to be important in the etiology of multiple sclerosis as the second cause of neurological disability in young adult population. Among them, trace elements such as magnesium (Mg) and zinc (Zn), because of their role in peroxidation and myelin injury, have been studied in different surveys. Hence, this study was designed to evaluate the plasma and cerebrospinal fluid (CSF) level of Mg and Zn in Iranian MS patients and to compare the concentration among patients with different clinical manifestation of disease.

Materials and methods: Twenty-six clinically definite MS patients attending neurology department of Sina hospital and 25 healthy controls living in the same geographical area were enrolled in the study. Cerebrospinal fluid and blood samples were obtained from both groups and analyzed for levels of Mg and Zn. Results: The mean serum level of Mg and Zn were 2.4027 ± 0.28927 mg/mL and 101.4 ± 2.4335 μg/mL in MS patients, respectively. These values in CSF were 2.4335 ± 0.24962 mg/mL and 4.3796 ± 1.77019 μg/mL, respectively. We could not find any significant difference between plasma and CSF levels of Mg and Zn in patients when compared to the control group. In addition, there were no significant association between the level of Mg or Zn and the clinical manifestation of the disease. Conclusion: Although trace elements theoretically may interfere with pathogenesis of the disease, the serum and CSF levels of Mg and Zn were not different between MS patients and the control group in our study.

IL-25 exclusively expressed by brain endothelial cells repairs
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Interleukin (IL)-25 is a member of the IL-17 family of cytokines including IL-17A and IL-17F. IL-25 mRNA is expressed in the whole brain tissue of normal mice. However, the cellular source of IL-25 and its function in the brain remains unclear. Here we show that the brain endothelial cells (BECs) exclusively express IL-25 in the central nervous system. IL-25 expression decreases with inflammatory cytokines such as tumor necrosis factor (TNF-α, IL-1β, IL-17, and IFN-γ) and is also downregulated in the inflamed brain. Stimulation with IL-25 induces the expression of tight junction proteins, occludin, junction adhesion molecule, and claudin-5. IL-25 restores the reduced expression of tight junction proteins, occludin, junction adhesion molecule, and claudin-5, induced by TNF-α, IL-1β upregulation of claudin-5 is inhibited by protein kinase C ε (PKCe) inhibitor peptide and PKCe phosphorylation is induced in the IL-25-stimulated BECs. These results suggest that IL-25 produced by the BECs regulates blood brain barrier (BBB) formation and protects against inflammatory cytokine-induced excessive collapse of the BBB through the PKCe-dependent pathway. These novel functions of IL-25 in maintaining BBB integrity may help us understand the pathophysiology of inflammatory brain diseases such as multiple sclerosis.

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P.26
CinnoVex, a Biosimilar Product for Treatment of MS
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Interferons are soluble glycoproteins that modulate immune responses. There are various different interferons which have quite different effects on the inflammation process in multiple sclerosis (MS). Treatment with interferon beta has helped patients with established multiple sclerosis. Three different forms of interferons (Avonex, Rebetol, and Betaseron) have been approved for treatment of MS. A biosimilar form of Avonex called CinnoVex has been manufactured and received approval from Ministry of Health and Medical Education of Iran. CinnoVex is produced in CHO cells and its physico-chemical and biological characteristics completely comply with the first draft of European Pharmacopoeia for this product. Two clinical studies have been done on CinnoVex. The first study is a double-blind randomized clinical trial comparing CinnoVex with Avonex in relapsing-remitting MS and the second study is an open-label, post-marketing study on 1050 relapsing-remitting MS patients receiving CinnoVex. The clinical trial was designed to test inferiority of CinnoVex compared to Avonex. Patients were followed by relapse rate, Expanded Disability Status Scale changes, adverse events, brain magnetic resonance imaging changes (T2 plaques count, plaque volume, number of Gd-enhancing lesions), and neutralizing antibodies (Nabs). The 12-months analysis has been performed on all patients and no significant difference was seen in any of the outcome measures between two groups. The study will be continued until all patients complete 24 months of follow-up.

P.27
Predictors of clinical response to interferon ?1b therapy in patients with multiple sclerosis
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Interferon-?1b (IFN-?1b) is effective in reducing relapses in multiple sclerosis (MS). However, some patients show a poor response to this drug. The aim of this study was to identify clinical, magnetic resonance imaging (MRI), and biological markers predictive of clinical response to IFN-?1b therapy in MS patients. Ten patients treated with IFN-?1b were followed over a two-year period. We compared clinical and laboratory data, including anti-aquaporin-4 (AQP4) antibody, longitudinally extensive transverse spinal cord lesions (LESCLS) extending over three vertebral segments, in these patients grouped as five patients experiencing relapses and five relapse-free patients. Also, we have investigated the expression of Th1-related CXCR3 chemokine receptors and Th2-related CCR4 chemokine receptors on T cells derived from patients undergoing IFN-?1b therapy. Conventional MS was significantly more common in the no-relapse patients than in the relapse patients, and the no-relapse patients did not show LESCLS from MRI. In addition, the no-relapse group showed lower Kirtzke’s expanded disability status scale scores, shorter disease duration, a greater number of relapses in the year prior IFN-?1b treatment, and a markedly lower frequency of auto-immune antibodies, including anti-AQP4 antibody. Treatment with IFN-?1b reduced the percentage of CXCR3-expressing CD4 T cells in both groups during the first 12 months. At 24th months after the treatment, the CXCR3 expression for non-relapse patients was still reduced. However, for relapsed patients it returned to a level at baseline. Clinical findings preceding the therapy, spinal cord MRI findings, or frequency of auto-immune antibodies may be the predictors of response to IFN-?1b therapy.

P.28
No increased incidence of exacerbations in patients with neuromyelitis optica during the first 90 days of treatment with interferon ?1b
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Recent studies showed that 5 of 10 Chinese patients with optic neuritis relapsed following interferon ?1a (IFN?1a) treatment, and two Japanese patients with neuromyelitis optica (NMO) had exacerbation in the first 90 days of interferon ?1b (IFN?1b) treatment. We investigated the frequency of exacerbation increases in the first 90 days of IFN?1b treatment in NMO patients. We conducted a retrospective study by examining the medical records of consecutive 71 classic multiple sclerosis (MS) and 38 NMO patients treated with IFN?1b. Twenty-four patients (14 MS and 10 NMO patients) had exacerbation in the first 90 days of treatment. These 24 patients did not show an increase in the frequency of exacerbation in the first 90 days of treatment. During 90 days after treatment, 14 MS patients (19.7%) and 10 NMO patients (26.3%) had one exacerbation event each. Classic MS patients showed a decreased frequency of exacerbation after treatment. NMO patients showed a slight decrease in the frequency of exacerbation, but was not significant. In all, 7 of 18 seropositive and 6 of 20 seronegative patients with NMO had exacerbation early after the treatment. No correlation between exacerbation after the treatment and the seropositivity for the anti-aquaporin-4 antibody was found. Several patients with optic neuritis or NMO had exacerbation early after treatment with IFN?1b; however, statistical analyses have not been carried out. Our results showed no increased incidence of exacerbations in NMO patients during the first 90 days of treatment with interferon ?1b.
NMO & autoimmune aquaporinopathy

P-31
The seroprevalence of NMO-IgG in Singapore – a pilot study

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Objective: To determine the frequency of neuromyelitis optica (NMO)-IgG in Singapore Patients with multiple sclerosis (MS), transverse myelitis or optic neuritis. Background: MS among Asians is often characterized by severe and selective involvement of optic nerve and spinal cord and is sometimes called opticospinal MS (OSMS). A novel autoantibody, NMO-IgG is present in NMO patients and Japanese OSMS patients, occurring at a frequency of between 55.6 and 73% of cases. The seroprevalence of NMO-IgG among Singapore patients is unknown. Design/Methods: Serum NMO-IgG was detected by identifying the distinctive staining pattern in mouse cerebellum by indirect immunohistochemistry. Our study included 11 patients with MS or syndromes at high risk of developing the disorder and 20 additional control patients who were either healthy or had miscellaneous autoimmune or neurological disorders.

Result: Of 11 patients with NMO/OSMS, 68% had a syndrome suspicious for NMO, 28% had OSMS. 13/18 patients (72%) had a moderate or marked improvement within 1–5 months of treatment. Severe TM and ON had similar response to treatment. Some of those with AQP4-Ab positive group showed only recurrent optic neuritis or only recurrent myelitis for several years. Our large series study clearly confirmed the characteristic features of AQP4-Ab positive group.

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Poster Presentations 145

P-30
Mitoxantrone rescue protocol for Canadian Asians with malignant demyelination

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Background: Canadian Asians with MS have a worse prognosis than Caucasians, especially those with opticospinal (OSMS) and neuromyelitis optica (NMO) like phenotypes. Spontaneous recovery or response to high-dose steroids for severe attacks of optic neuritis and transverse myelitis can be poor. Less than 50% of patients respond to plasmapheresis (PLEX). Objective: To assess short-term clinical outcome for severe episodes of demyelination treated with a mitoxantrone (Vancouver Rescue Protocol). Methods: Open label, unblinded assessment of patients with a severe episode of demyelination and no improvement after a course of IV methylprednisolone (1gram IV x3 days) or failed PLEX. We used the Mayo Clinic global outcome score: no improvement, mild improvement without impact on function, moderate improvement, marked improvement. Results: 14 patients with 18 severe relapses of acute demyelination were treated with mitoxantrone rescue (20mg/m2 monthly for three treatments). 55% were East Asian, 11% South Asian and 28% Caucasian. 68% had a syndrome suspicious for NMO, 28% had OSMS. 13/18 (72%) had a moderate or marked improvement within 1–5 months of treatment. Severe TM and ON had similar response to treatment. Conclusion: Severe relapses are common in Asian MS and associated with a poor recovery and prognosis. High-dose steroids or PLEX is only effective in some patients. The Vancouver Rescue Protocol with mitoxantrone following a poor response to steroids and PLEX requires further validation in a larger population. However, it suggests that potent immune suppression may lead to improved recovery in Asians with OSMS or NMO like syndromes.

P-32
Anti-aquaporin 4 antibody test in a large series of Japanese NMO/OSMS

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We established the immunofluorescence detection system of neuromyelitis optica-igG using rat brain cryostat sections and AQP4 antibody (AQP4-Ab) test using human AQP4-transfected HEK 293 cells and examined 2076 sera or cerebrospinal fluid (CSF) sent to our institute since 2006. Among them, 569 sera/CSF were positive for AQP4-Ab (27.4%). 450 of AQP4-Ab positive sera/CSF were from women (79.1%). Clinical and laboratory features of AQP4-Ab positive or negative patients were compared. AQP4-Ab positive group showed higher onset age, higher percentages in blind and bed-ridden patients, higher Expanded Disability Status scores, 75% of them showed long spinal cord lesions more than three vertebrate segments on spinal MRI. However, the positivity of other systemic autoantibodies such as anti-nuclear antibody or existence of cerebral or brain stem lesions on MRI were not different between AQP4-Ab positive and negative group. Some of those with AQP4-Ab positive group showed only recurrent optic neuritis or only recurrent myelitis for several years. Our large series study clearly confirmed the characteristic features of AQP4-Ab positive group.

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P-34
Hypercomplementemia at relapse in patients with anti-aquaporin-4 antibody
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Opticospinal multiple sclerosis (OSMS) in Asians has similar characteristics to relapsing neuromyelitis optica. As both groups of patients frequently have anti-aquaporin-4 (AQP4) antibody, complement-mediated disruption of astrocyte foot processes is proposed, but not yet proven. In this study, we aimed to clarify whether complement consumption occurs at relapse in anti-AQP4 antibody-positive patients. We analyzed serum CH50, C3, C4, and C-reactive protein (CRP) levels and their relation to clinical phases in 118 MS patients with or without anti-AQP4 antibody. Serum CH50 levels were higher in 24 patients with anti-AQP4 antibody than in 39 OSMS and 34 conventional MS (CMS) patients without anti-AQP4 antibody at relapse (Pcorr<0.05), but not in remission. The frequency of hypercomplementemia (CH50 higher than 50 U/ml) at relapse was also higher in anti-AQP4 antibody-positive patients than in anti-AQP4 antibody-negative CMS patients (70.4% vs 29.0%, Pcorr<0.05). C3 and C4 levels did not differ significantly among the three groups at relapse. In patients with anti-AQP4 antibody, coexistence of both hypercomplementemia and high CRP values was more common at relapse than in the remission phase (36.0% vs 10.5%, P < 0.05). In patients with extensive central nervous system lesions, hypercomplementemia was significantly more common in anti-AQP4 antibody-positive patients than the antibody-negative ones (88.9% vs 16.7%, P < 0.01). We consider that hypercomplementemia in anti-AQP4 antibody-positive patients may reflect a systemic inflammatory reaction at relapse.

P-35
CSF and peripheral blood cytokine production profiles and HLA class II alleles in patients with antibody to aquaporin-4
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Objectives: To clarify cytokines and HLA class II alleles associated with the presence of antibodies to aquaporin-4 (AQP4) in Japanese opticospinal multiple sclerosis (OSMS) patients. Methods: We studied serum AQP4 antibody titers in 148 clinically definite MS patients and their relationships with extra- and intra-cellular cytokine production profiles in peripheral blood and cerebrospinal fluid (CSF), and HLA-DPB1 and -DQB1 gene polymorphisms. Results: CD4+IFN-γ+IL-4+T cell percentages in peripheral blood were significantly higher in anti-AQP4 antibody-negative OSMS patients than positive ones. CD4+IFN-γ+IL-4+ and IFN-γ+IL-4+T cell percentages showed a significant negative correlation with anti-AQP4 antibody titers. In CSF cells, CD4+IFN-γ+IL-4+T cell percentages were significantly higher in anti-AQP4 antibody-positive patients than the antibody-negative ones. In CSF, IL-4, IL-8, IFN-γ, tumor necrosis factor α levels were significantly higher in patients with OSMS than patients with CMS and those with other non-inflammatory neurological diseases, irrespective of the presence or absence of anti-AQP4 antibodies. The phenotypic frequency of the HLA-DPB1*0501 allele was significantly increased in anti-AQP4 antibody-positive patients compared with healthy controls, but not in the antibody-negative OSMS patients. Conclusion: These findings suggested that anti-AQP4 antibodies are produced as a result of a heightened Th2 response and the presence of the HLA-DPB1*0501 allele in Japanese.

P-36
Analysis of cytokine and chemokine in multiple sclerosis and neuromyelitis optica
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Background: In conventional multiple sclerosis (CMS), the Th1 cell upregulation is seen during relapse. As Th1 level in neuromyelitis optica (NMO) is higher than the control group, Th2 level is significantly higher than CMS. Objective: To describe Th1/Th2 balance of cerebrospinal fluid (CSF) in serum NMO patients during disease activity. Method: In this study, we analyzed CSF cytokine and chemokine in CMS and NMO patients. The number of patients was 10 and 7. A control group was composed of 10 noninflammatory disease patients. Cytometric Bead Array (CBA, Biorad) was used to detect cytokines and chemokines. Analysis were performed for IL-2, IL-4, IL-6, IL-10, TNF-α, IFN-α, CXCL8/IL-8, CXCL9/MIG, CXCL10/IP-10, CCL5/RANTES, and CCL2/MCP-1. CSF IL-17 was not analyzed. Result: IL-6 and IP-10 in NMO were inclined to show high level than in CMS and control. Although TNF level and IL-10 level in NMO and CMS were higher than that of control, there was not significant difference between in NMO and in CMS. Conclusion: Our findings suggest that there is some certain tendency of cytokine/chemokine towards in NMO in CMS.
Anti-AQP4 antibody was measured by a high-sensitive assay using HEK-293 transfected with AQP4 and indirect immunofluorescence method (Takahashi T, et al. Brain 2007; 130:1235). Among the eight series of PE, seven sufficiently reduced the anti-AQP4 titers even after HDMP therapy. The clinical improvement usually started to appear after one or two exchanges. Reducing anti-AQP4 antibody seems to be relevant to the therapeutic efficacy. Low-dose administration of oral prednisolone (10–15 mg/day) and/or immune suppressants, such as azathioprine (100 mg/day), after PE maintain the anti-AQP4 antibody titers at low levels as we previously reported (Takahashi T, et al. Brain 2007; 130: 1235, Watanabe S, et al. Mult Scler. 2007;13:968).

Related disorders

P-39

Clinical, laboratory, MRI, and electrophysiological findings in acute transverse myelitis: comparison between patients with and without multiple sclerosis

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Background: Acute transverse myelitis (ATM) is a pathogenetically heterogeneous inflammatory disorder affecting the spinal cord at one or more segments. Therefore, the identification of discriminatory findings providing clues of the underlying etiologies is needed. Moreover, there is paucity of comparison studies correlating the MRI and electrophysiological changes in ATM with and without multiple sclerosis (MS). In Korea, the spinal cord is the most commonly affected site of MS and its clinical features often resemble those of ATM. As the prognoses of these two conditions are different, it is important to distinguish them from each other. The purpose of this study was to evaluate discriminatory findings that could help differentiate ATM from MS.

Methods: We analyzed the clinical, imaging, electrophysiological, laboratory findings, and outcome profiles in myelitis with and without MS. Results: We identified 70 patients and compared non-MS-related ATM (ATM, n = 52) to myelitis associated with MS (ATM-MS, n = 18). The ATM patients were significantly older than ATM-MS patients at the time of the diagnosis (P < 0.05). A motor weakness was more frequent in ATM than in ATM-MS where symptoms were predominantly sensory (P < 0.05). Spinal cord MRI revealed monosegmental involvement of spinal cord was more frequent in ATM-MS, in contrast to ATM, where lesions involved two or more vertebral levels (P < 0.05). Cerebrospinal fluid oligoclonal bands were frequent in ATM-MS but not statistically significant. Abnormalities (assessed by summation of number of abnormal studies) of neurophysiological tests including visual evoked potential (VEP), brain stem auditory evoked potential (BAEP), and median and tibial somatosensory evoked potentials (SEP) are more frequent in ATM-MS (P < 0.05). Clinical outcomes defined on the basis of three or more vertebral levels modified Rankin scale was better in ATM-MS than in ATM (P < 0.05). Conclusion: ATM and ATM-MS may be differentiated on neurophysiological and outcome data, and these findings may provide therapeutic implications for patients with myelitis.

P-40

Clinical, laboratory and radiological manifestations of atopic myelitis in Korea

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Background: HyperIgEaemia and atopy have recently been reported to be related with various neurological diseases including myelitis. The aims of this study are (1) to determine frequency of atopic myelitis (AM) in Korea and (2) to characterize the clinical profiles of the disease entity. Method: From January 2006 to August 2008, 29 patients with idiopathic myelitis were recruited. We compared demographic data, laboratory results, and radiologic findings between patients with atopic diathesis and those without. Results: Of 29, 14 AM patients (48%) were identified. Allergic or atopic history was found in only four patients (13%), but hyperIgEaemia and antigen-specific IgE were observed in 17 (58%) and 19 (65%), respectively. Patients with AM showed following distinctive features: (1) younger age at onset (39 years vs 51 years; P < 0.0001), (2) non-acute onset (13/14 vs 5/15; P = 0.002) and long duration of symptoms at admission (76 days vs 16 days; P < 0.001), (3) predominant sensory symptoms with mild weakness (4) low Expanded Disability Status Score (2.1 vs 5.6; P < 0.001), (5) low frequency of abnormal SEP findings (2/14 vs 11/15; P = 0.0013), and (6) increased eosinophil in peripheral blood (5.0% vs 1.0%; P < 0.001). MR findings of AM were characterized by eccentric lesions occupying more than two-thirds of the spinal cord (92%) with focal peripheral enhancement (92%) on axial images, and by relatively long lesion extending three to five vertebral segments (71%) with swelling (71%). Conclusions: Patients with AM are fairly common in Korea and had relatively homogenous clinico-laboratory and radiological features.

P-41

Toxocara canis myelitis: similar clinical features to atopic myelitis

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Background & Objective: Atopic myelitis is defined as myelitis of unknown cause with atopic diathesis or mite-specific hyperIgEaemia. Toxocariasis is a zoonotic infection caused by toxocara canis. This study is to investigate toxocara infestation in patients with clinically suspected atopic myelitis. Methods: We retrospectively examined ELISA study for toxocara canis in serum of patients with myelitis and hyperIgEaemia. Specific IgG antibody to toxocara excretory-secretory (TES) antigen was measured by toxocara ELISA. Clinical, laboratory, and MRI findings were analyzed. Results: Forty-one patients with atopic myelitis were included. The mode of symptom onset was subacute/chronic in 36 patients and acute in five patients. Raw food history within six months was found in 25 patients (71%). Presenting symptoms were characterized by paresthesia/dysesthesia (31/41, 75%), weakness (11/41, 75%), and sphincter dysfunction (4/41, 9%). Almost all patients (38/41, 93%) had increased serum IgE (2502.5 ± 5196.8 U/mL). Allergen-specific IgE level was increased (16/32, specific IgE to Dermatophagoides pteronyssinus, and 29/32, specific IgE to D. farinaceae). There was eosinophilia in peripheral blood (22/41, 54%). Specific IgG antibody to TES antigen was increased (26/30, 87%). Lesion length in spine MRI was 3 ± 2.3 segments. Cord swelling (39/41, 75%) and enhancing lesions (29/41, 72%) were frequent findings. Clinical course was step-wise progression despite intravenous high-dose methylprednisolone (28/41, 68%). Conclusions: In our retrospective study of 41 patients with clinically suspected atopic myelitis, 87% of patients were positive IgE antibody. Screening of toxocara canis infection in atopic myelitis should be considered.
The clinical characteristics and MRI findings in Neuro-Behcet's disease.

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Behcet's disease, a chronic multisystem inflammatory disorder of unknown etiology, rarely involves central nervous system (CNS) and manifest an isolated leptomeningeal inflammation (MS) with relapsing–remitting pattern and multiple separated lesions. The authors investigated the clinical characteristics and MRI findings in neuro-Behcet's disease (NBD) by reviewing the charts of 64 cases as diagnosed having NBD over 10 years. A total of 42 patients fulfilled the criteria proposed by International Study Group for Behcet's disease in 1990. Four of them had cerebral vascular event or dural sinus thrombosis and regarded as secondary CNS involvement. Remaining 38 cases (17 men, 21 women) were evaluated. The most common symptoms were pyramidal signs, headache, ataxia, dysarthria, and diplopia. Thirteen (34.2%) had recurrent attack and three of them were initially diagnosed with MS. MRI revealed more than one CNS lesion in 34 (89.5%) patients and brainstem, basal ganglia, and subcortical white matter were most frequently affected. Most of the lesions were dot-like or streaky but, tumefactive in one case. Brainstem atrophy was not infrequent in our study, and in one case, the only abnormal finding was diffuse brain, brainstem, and spinal cord atrophy. Seventeen (48.6%) patients had myelopathy. Cerebrospinal fluid (CSF) study was performed in 18 patients and all of them were abnormal but one. In conclusion, NBD is one of the important differential diagnoses of chronic recurrent neurologic disorder, and MRI and CSF study may be helpful.

Case presentation

P-43

Classic Western multiple sclerosis in Mongolia: clinical case study with magnet resonance image and visual evoked potential

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Background: Multiple sclerosis (MS) is uncommon disease in Mongolia. For the first time, we reported classic MS case. It has been diagnosed by using McDonald's diagnostic criteria, Kurtzke's Expanded Disability Status Scale (EDSS), functional system (FS), magnetic resonance image (MRI), and evoked potential (EP). Case description: A 28-year-old woman has blindness, weakness in right foot, urinary incontinence. The onset presented at 26 years in September 2006 with pain and abnormal sensation in upper extremities. Next exacerbation with visual impairment more in left eye has been diagnosed in December 2006 after three months of onset. In January 2007, the patient had burning sensation in lower extremities. Sensory impairment reduced after some days without treating. The course of MS was stable from February to July 2007. There were any exacerbations. Next exacerbation presented in August 2007 with urinary incontinence, and gait ataxia. The MS symptoms had reduced after treating by methylprednisolone. Now the patient has RR MS with EDSS 4.0, FS 14. T2-weighted and FLAIR MRI of brain revealed hyperintensive different sized heterogeneous lesions in the white matter of both cerebral hemispheres mainly in periventricular region. For the spinal MRI, the patient had two lesions in cervical segment. Visual evoked potential (VEP) was revealed an increasing latency P100 in left side. Conclusion: We report Western form MS case due to McDonald diagnostic criteria, MRI, and VEP for the first time. Mongolia is an Asian country. In spite of that we conclude the Western MS may be found among Mongolians.

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A variant of MS or early MS?  
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Backgrounds: Acute longitudinal myelitis is a group of disorders characterized by multifocal or long segmental inflammation of the spinal cord. We present a 30-year-old man with progressive paraparesis with longitudinal spinal cord lesion but no evidence of connective tissue disease or multiple sclerosis. Case: A 30-year-old man presented with progressive paraparesis which began four days before admission. His neurological deficits occurred abruptly and showed rapid progression to paraplegia, neurogenic bladder only within two days. The sensory deficit was occurred below T4 level. Laboratory data showed no evidence of connective tissue disease. Aspirated cerebrospinal fluid contained 432 WBC/µL, protein 92.2 mg/dL. IgG index was 0.8. Somatosensory evoked potential findings were suggestive of central conduction defect. But visual evoked potential findings were normal. MRI of the whole spinal cord showed multifocal high signal intensities involvement. After start of steroid therapy, weakness was rapidly progressed. It was non-specific findings. After administration of intravenous methylprednisolone for five days, paraparesis and sensory deficits have recovered to almost normal state over two weeks. But voiding difficulty has not improved. Follow-up MRI performed one month later revealed markedly decreased high signal intensities. Conclusion: We report a case of acute idiopathic longitudinal myelitis which was not accompanied by other connective tissue diseases such as SLE or Sjögren's syndrome and showed dramatic response to steroid therapy. Therefore, in these diseases, it is important that the possibility of multiple sclerosis should be kept in mind during follow-up.

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Successful Treatment with Plasma Exchange in a Patient with Neuromyelitis Optica with Extensive Brainstem Lesions Leading to Coma

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Background: Early and accurate differentiation of neuromyelitis optica from multiple sclerosis is critical because the former carries a poorer prognosis and the therapeutic approach differs. Case: A 32-year-old woman visited our hospital because of the recent development of tight banding like sensation around the trunk. She was previously diagnosed as having multiple sclerosis and taking intramuscular therapy, and on β2b. Her first attack was at 17 years before admission with right optic neuritis and hemiparesis, followed by three attacks. On neurological examination, right-sided blindness and paresthesia of bilateral T6 to T10 level were observed with pyramidal signs. The cerebrospinal fluid study revealed pleocytosis and elevated protein level. We first started methylprednisolone. However, she began to rapidly deteriorate. The brain MRI demonstrated multiple new high signal intensities in T2WI. The spine MRI also demonstrated an extensive high signal lesion from upper thoracic cord to conus medullaris in T2WI. In none of the lesion, no contrast enhancement was observed. In a week, she fell into coma with loss of brainstem reflexes. As the neuromyelitis optica (NMO) IgG antibody returned as positive, we started plasma exchange. Two days after plasma exchange, she began to respond and became fully conscious with the improvement of her brainstem signs. She also re-attained motor functions two months later and was discharged. Conclusions: Our case support the idea that NMO can have symptomatic brain lesions, which may lead to coma, and the plasma exchange is an important therapeutic option in NMO, especially when the patients do not respond to steroid.

Late-onset Krabbe’s disease presenting as the myelopathy

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The Krabbe’s disease that affects both the central and peripheral nerve system is caused by genetic defects of galactocerebrosidase. Usually, this disease occurs in the infant period, but rarer late-onset forms also exist. We report an unusual case of late-onset Krabbe’s disease that presented with sensory abnormalities in the thoracic level. A 53-year-old woman complained of progressive worsening pain in her trunk for three years. She received esophagogastropathy due to a suicidal attempt. She showed spasticity in the legs, hyperesthesia to pain and temperature in the T3-T10 sensory level, and a mild decrease of cognition. As her vitamin B12 was low (166 µg/dL), IM cobalamin was given to the patient but with no effect. A spine MRI only revealed a compression fracture of the T12 vertebral body. Cerebrospinal fluid (CSF) and EP studies were normal. A brain MRI demonstrated white matter demyelinated changes (Figure). She was diagnosed with Krabbe’s disease due to markedly reduced activity of galactocerebrosidase in the leukocytes (Table). This is the interesting case of a patient with Krabbe’s disease whose symptoms occurred in the adult period and resembled myelopathy. We suggest that Krabbe’s disease is clinically heterogeneous disease, and laboratory findings and cerebral image are necessary to exclude other disorders.

An adult case of multiphasic disseminated encephalomyelitis (MDEM)

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Background and Significance: Acute disseminated encephalomyelitis (ADEM) is a monophasic autoimmune demyelinating disease of the CNS. However, it has been reported that 25 to 33% of ADEM patients experience relapses. In the cases of relapse, the differential diagnosis of MDEM (multiphasic disseminated encephalomyelitis) from MS (multiple sclerosis) is very obscuring. Case: A 37-year-old man admitted due to headache, nausea, and vomiting. The cerebrospinal fluid (CSF) finding was polymorphic neutrophil dominant lymphocytosis. Initial clinical diagnosis was the bacterial meningitis, so he was treated with intravenous antibiotics. On fourth day, he developed right-leg weakness. The MRI T2-weighted image showed multifocal high signal intensities on the pons, midbrain, basal ganglia, and corona radiata. The myelin basic protein, the IgG index was within normal ranges and the oligoclonal band was negative. He was diagnosed with ADEM and treated with oral prednisolone, and the weakness improved. On tapering of corticosteroid slowly, he showed no neurologic manifestations. Eleven months after discontinuance of treatment, he had headache, nausea, vomiting, and ataxia. The CSF study findings were similar to the previous results. There were newly developed lesions in the basal ganglia and pons on the brain MRI, and there were no significant findings on the whole spine MRI. He was treated with intravenous methylprednisolone, and the symptoms were improved. Discussion and Comment: MDEM is one of the chronic forms of ADEM. The differential diagnosis from MS is very difficult. But the viral prodrome, early-onset ataxia, high lesion load on MRI, involvement of deep gray matter, and absence of CSF oligoclonal bands, the history of dose reduction or discontinuance of treatment are more appropriate for MDEM than MS. We do not know yet MDEM is a different disease with MS or the part of same demyelinating spectrum. More follow-up studies of the patients diagnosed as having MDEM will be helpful for revealing the pathogens.

Moyamoya disease with Brain MRI patterns of Multiple Sclerosis

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Background: Every diagnostic criteria of multiple sclerosis have a critical limitation in the specificity and the sensitivity. MRI is one of the most important studies because this can document the dissemination of time as well as space. But sometimes MRI study can lead misdiagnosis if we neglect the fact that MR finding is only nonspecific. Here we report a case of moyamoya disease misdiagnosed as multiple sclerosis because of MR abnormalities. Case: A 29-year-old man visited to local hospital with recurrent left-hand weakness. Left-hand weakness developed in October 2006 at first followed by recurrent symptom more than 10 times for three months which lasts about 4-5 hours. He lost left vision at 2004 due to trauma. Four months before, dizziness appeared for 10 days after exercise. There is no other medical history. MRI showed multiple white matter lesions in right hemisphere including one gadolinium-enhancing focus (Fig 1). He was transferred to this hospital for the treatment of multiple sclerosis. On admission, a neurologic examination showed no motor and sensory deficits. On the 2nd hospital day, dysarthria and left-side weakness appeared and continued about four hours. For evaluation of vascular disease, brain angiography performed which showed the moyamoya disease (Fig 2). Conclusion: We report a case of moyamoya disease in young man who showed multiple white matter lesions in brain mimicking MS. If clinical manifestations are atypical for MS, the possibility of other disease has to be excluded even though showing typical MRI pattern of MS.