POSTERS – NEUROLOGY

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Recombinant forms of myelin antigens expressed on CHO cells as a tool for identification of autoantibodies in serum of MS patients

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Introduction/Objectives: An important contribution of B cells and autoantibodies has been demonstrated in the pathogenesis of multiple sclerosis (MS) leading to interest in the use of such autoantibodies as diagnostic or prognostic markers. A common problem in studies of humoral immunity is that accurate detection of antibodies depends highly on the conformation of the antigens used for detection. Therefore widely used techniques, including ELISA and Western blotting, may fail to detect reactivity against epitopes displayed by native antigens expressed on myelin sheats. Here we describe a cell-based assay that specifically identifies serum antibodies directed against three major myelin autoantigens: MBP, PLP and MOG. The proposed method detects antibody binding to recombinant antigens in their native conformation on MBP, PLP and MOG transfected mammalian (hamster ovary) cells.
Material and methods: Thirty-six patients with relapsing-remitting MS diagnosed according to criteria of Mc Donald were recruted. Age 38.2 and duration of the disease 7.1. Serum anti-MBP, anti-PLP and anti-MOG IgG autoantibodies were detected in MS patients and 35 healthy donors by FACS analysis.
Results: Compared with healthy controls the titers of IgG autoantibodies directed against membrane-bound recombinant myelin antigens were most significantly increased for PLP ($P < 0.0001$), no quite significant for MBP ($P < 0.05$) and not significant for MOG ($P < 0.7$). The titers of anti-MBP antibodies were low indicating low concentration of these Ab in serum of MS patients and healthy donors, in contrast to high titers of anti-MOG antibodies in both groups suggesting a non-specific binding.
Conclusions: The cell-based assay detection of autoantibodies directed against recombinant myelin antigens could be a useful tool providing the serological markers in diagnosis and progression of MS. Indeed, it could allow to obtain molecular characteristics of disease in each patient in term of an antibody response against certain myelin and non-myelin antigens. We have shown that in RRMS patients elevated level of serum antibodies against PLP is significant, what should be considered in search for specific immunomodulatory therapy in MS.

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Cytogenetic analysis of MSRV POL, GAG, ENV sequences and genome instability in multiple sclerosis

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Introduction/Objectives: Among of the potential agents causing multiple sclerosis MSRV virus (multiple sclerosis-associated retrovirus) is often taken into consideration. Aims of the study were 1) an assessment of MSRV potential role in MS and 2) test of genome instability in MS patients.
Participants, Materials/Methods: The material was peripheral blood lymphocytes from 92 patients with MS, 12 patients with myasthenia and 20 healthy persons. The FISH studies with labeled PCR products of pol, gag and env MSRV genes in nuclei, chromosomes and chromatin fibers were done. Classical cytogenetic techniques were introduced into karyotypes and micronuclei analyses. MSRV pol, gag and env sequences were found in both MS patients and controls.
Results: The copy number of MSRV pol sequences was significantly greater in MS patients (6–24 copies on nucleus) than in myasthenia (4–5 copies) and normal individuals (3–6 copies). MSRV gag sequences was found in a range of 5–20, 4–5 and 2–4 copies in MS patients, patients with myasthenia and healthy donors, respectively. MSRV env was found in a range of 6–22, 4–5 and 2–4 copies in MS patients, patients with myasthenia and healthy donors, respectively. Moreover, the number of spontaneous micronuclei was significantly greater in MS patients compared to control. In patients with MS diversity of chromosome aberrations was observed.
Conclusions: In conclusion, evident difference in MSRV pol, gag and env copy number between MS patients and control suggests that MSRV may play some role in the etiology of multiple sclerosis (latent viral infection). The presence of chromosome aberrations and high amount of micronuclei in MS patients shows that the instability in MS genome often occurs.

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Review of multiple sclerosis at the neurology clinic in Sarajevo during 2006

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Introduction/Objectives: Multiple sclerosis is one of the most common, most difficult and most important neurological diseases, because of its frequency, chronic features and tendency to affect young people. In Bosnia and Herzegovina there is no register of patients with MS. In the Sarajevo Canton there are 198 registered patients, who are treated in the Clinical Center of

Sarajevo University. Care for patients at the Neurology Clinic of Clinical Center Sarajevo is partly of secondary, and partly on tertiary level of health care. Tertiary level of care is for the patients from 4 Cantons.

Goal: To provide a review of the population suffering from multiple sclerosis treated during 2006 at the Neurology Clinic of Clinical Center of Sarajevo University from the aspect of gender differences, age, type of disease, average duration of hospitalization, precipitating factors for the disease or relapsing, and noticed mental disturbances. Particular emphasis is given to the treatment with immune system modulators.

Participants, Materials/Methods: In this study we used a specially designed questionnaire, and history of illness of patients who were diagnosed as multiple sclerosis, treated at the Neurology Clinic from January 1st – December 31st 2006.

Results: The number of patients with MS was 71 (61.87% of female gender) aged from 40–49 years (43.66%). The average lifetime with respect to the onset of the first symptoms was 33.01 ± 8.3 years. Hospital stay lasted on average of 19.5 days. Precipitating factor in 29.57% of cases with deterioration or disease is the infection and in 16.9% the stress. 26.76% of patients had a RR type of illness. Therapy with interferon was in 4.48% of patients. Therapy with high doses of metilpredinisolone received 66.7% of patients. Depression disorder was present in 32.9% of patients, and cognitive dysfunction in 9.86%. The average EDSS score was 4.5. Relapsing rate was 4.63 per patient.

Conclusions: Based on our research we can conclude that the overall mortality of clinical patients, MS was responsible for 2.84% of all treated. Average patient's age was 33.01 years with a statistically significant more frequent disease in female population. Average EDSS was 4.5, relapsing rate 4.63, the possibility for immune modulating therapy 4.48%. In the next period is imperative to create a unified register of patients in order to conduct their treatment according to therapeutic guidelines.

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Differential down-regulation of soluble adhesion molecules during Natalizumab treatment

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Introduction/Objectives: Natalizumab (Tysabri) is a monoclonal antibody used in the treatment of multiple sclerosis (MS). This humanized antibody binds directly at the alpha 4-integrin subunit of the adhesion molecule (AM) very late activation antigen-4 (VLA-4) and thus leads to an inhibition of immune cell extravasation across the blood brain barrier. This consecutively results in a reduced inflammation of the central nervous system. Our objective was to study the effect of Natalizumab on soluble cell AMs in peripheral blood of patients before and 3 months after onset of Natalizumab treatment.

Participants, Materials/Methods: We determined serum concentration levels of four different AMs (soluble intercellular adhesion molecule-1, -2, -3 [sICAM-1, -2, -3] and vascular cell adhesion molecule-1 [sVCAM-1]) by using fluorescent bead immunoassay and enzyme linked immunosorbent assay (ELISA). Blood was sampled from 15 MS patients before and 3 months after onset of Natalizumab treatment.

Results: A significant decrease was found in all patients for the median of sICAM-3 serum concentration levels (before therapy: 100 ng/ml; after 3 months: 61 ng/ml; $P < 0.001$) and sVCAM-1 (before therapy: 580 ng/ml; after 3 months: 216 ng/ml; $P < 0.001$) levels 3 months after onset of Natalizumab treatment. In contrast, serum levels of soluble ICAM-1 (before therapy: 452 ng/ml; after 3 months: 479 ng/ml) and ICAM-2 (before therapy: 263 U/ml; after 3 months: 242 U/ml) remained unchanged.

Conclusions: We were able to show a differential effect after 3 months of natalizumab treatment with decreased serum levels in all investigated MS patients in two of the four investigated AMs (sICAM-3 and sVCAM-1).

VCAM-1 is the ligand of VLA-4. We therefore conclude that the decrease of sVCAM-1 might be a result of natalizumab mediated blocking of VLA-4. Alternatively, the decrease of sVCAM-1 in conjunction with the decrease of sICAM-3 might also be due to the anti-inflammatory effects of Natalizumab.

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Epidemiology of multiple sclerosis in Tuzla canton, Bosnia and Herzegovina

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Objective: To determine the incidence and prevalence of multiple sclerosis in the Tuzla canton, Bosnia and Herzegovina.

Patients and methods: The area of the Tuzla canton is 2649 km^2 and consists of 13 municipalities. After the war (1992–1995), there was no population census in Bosnia and Herzegovina. According to the report from Institute for statistics of federation Bosnia and Herzegovina in 2005, the Tuzla canton had an estimated population of 502 862 residents. Our Departmant of Neurology is the only one capable to diagnose and treat people suffering from multiple sclerosis in the canton. We have calculated the incidence and prevalence of Multiple sclerosis by analysing existing medical documentation (history of illness and hospital protocols).

Results: In the Tuzla canton total number of people suffering from Multiple Sclerosis (on 31.12.2008.) is 140, average age of 40.37 years (± SD 10.65). Average age of patients was 34.69 (± SD 10.54) years when the illnes was diagnosed. The youngest patient was 12 year old, and the oldest 73 years. Diseases were twice more frequent in women then in men (94; 67.1%/46; 32.9%). The prevalence was 27.84 patients per 100 000 population. The average incidence for the 10-year period (1999–2009) was 2.38/100 000. The lowest incidence was 0.59/100 000 population (1999), and the highest 4.78/100 000 population (2007).

Conclusion: The results show that the Tuzla canton belong to the area with a midlle prevalence of multiple sclerosis (upper limit). Moreover, the incidence of illnes has the tendency to increase in the last ten years.

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Brain white matter abnormalities in patients with Myotonic dystrophy type 1: is this multiple sclerosis?

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Introduction/Objectives: Myotonic dystrophy type 1 (DM1) is an autosomal dominant multisystemic disorder that affects skeletal and smooth muscle as well as the eye, heart, endocrine system, and central