Epidemiology and MRI

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Título / Title: Corpus Callosum Index: development of a Brazilian MRI marker on cell loss in MS

Introdução / Introduction: Current MS therapies target the newly defined concept of “no evidence of disease activity” (NEDA) with emphasis on the inflammatory activity of disease, defined by clinical relapses and EDSS progression, besides with absence of T1W contrast enhancing lesions as well as no new or enlarging T2W lesions on MRI. As cell loss seems to be a major determinant of disability, and may occur with lacking clinical expression, newly proposed inclusion of brain atrophy, NEDA 4, was defined by no more than 0,4% of brain volume reduction annually. This update required a systematic approach to measures of cell loss, which has complex demands and requires sophisticated methodology, not always available to most centers and difficult to be applied in real world. We propose a method, corpus callosum index (CCI), as practical option that measures atrophy and can be used in daily practice as a tool for optimal therapy.

Material e Método / Material and method: A retrospective analysis of published papers since 2001 and the development and validation of our method. Conventional MRI was obtained annually and serial CCI uses a mid sagital FLAIR sequences on a 2D simple orthogonal model. Results were compared intra patients, matched to EDSS and neuropsychological tests and normalized for validation. All studies used a control group, composed by non-inflammatory diseases.

Resultados / Results: After 15 years, we prospectively studied 217 RRMS patients (McDonald 2001). Besides our studies, about 30 international papers prospectively used CCI as marker for neurodegeneration. Recent study showed a good correlation between CCI and EDSS and SDMT, an accuracy of 94% to differentiate MS patients from controls and an overall (AUC) accuracy of 90%.

Discussão e Conclusões / Discussion and Conclusions: These data demonstrate that CCI can be a practical and feasible tool to follow MS patients, using conventional MRI sequences. We propose this parameter to be included as one requirement for "disease free" patient concept.

Palavras Chave / Key-Words: progressive MS, brain atrophy, CCI

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Instituições / Institutions: Instituto do Cérebro do Rio Grande do Sul - PUCRS - Rio Grande do Sul - Brasil, Serviço de Neurologia, Hospital São Lucas da PUCRS - Rio Grande do Sul - Brasil

Título / Title: Correlation of brain volume measuresand lesion load with neuropsychiatric tests in patients with multiple sclerosis

Introdução / Introduction: It is already known that cognitive dysfunction correlates with brain lesion load and tissue lossin patients with multiple sclerosis (MS). We aimed toinvestigate which tests from a comprehensive neuropsychological battery would show better correlation with MRI measures of brain volume and lesion load.

Material e Método / Material and method: As part of a broader, longitudinal study in relapsing-remitting MS, prospectively gathered patients' data was analyzed in this cross-sectional study.Brain images were obtained by using a 3.0 Tesla MRI scanner. Measures of whole brain (WBV), white matter (WMV) and gray matter (GMV) volumes were estimated independently by two software packages (Icometrix® and SienaX®).Lesion load was estimated by the Icometrix® software. An extensive neuropsychological battery was also done.

Resultados / Results: Sixteen patients were included. Time of disease onset ranged from 3 to 142 months (mean: 44) and EDSS scores ranged from 0 to 5. Statistical analysis demonstrated moderate correlation between SRT and WMV (r=0.579,p=0.019) and between SPART-D and GMV (r=0.522, p=0.038). Mean brain lesion load was 15.2 mL (range: 1.4-45.5). A strong inverse correlation (r=-0.691,p=0.004) between SRT and lesion load was found, as was a moderate inverse correlation (r=-0.623,p=0.013) between WLG and lesion load. There was a trend, not statistically significant, towards a moderate inverse correlation (r=-0.476,p=0.073) between SDTM and lesion load and between SPART-D and WBV (r=0.457,p=0.075).

Discussão e Conclusões / Discussion and Conclusions: In this study, only a few of the neuropsychological parameterscorrelated with MRI measures of brain volumes, perhaps because of the small sample size. Tests of verbal learning/memory and verbal fluency were the neuropsychological parameters associated with MRI brain lesion load in our sample. Further analyses with a larger number of patients are ongoing and may provide a better understanding on that matter.

Palavras Chave / Key-Words: Relapsing remitting multiple sclerosis, brain volume, lesion load, brain MRI, neuropsychiatric tests

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Forma de Apresentação / Presentation: POSTER

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Título / Title: DEVELOPMENT OF AN AUTOMATED METHOD TO IDENTIFY MULTIPLE SCLEROSIS LESIONS ON BRAIN MRI

Introdução / Introduction: Manual interaction in the task of multiple sclerosis (MS) lesion segmentation subjects the process to limitations that are widely discussed. Defining an automated method, therefore, presents the possibility of improving this procedure. The principle automated segmentation methods require the acquisition of multimodal magnetic resonance imaging (MRI) exams, which ultimately distances them from the reality of clinical practice. Given this scenario, the development of a method using only one MRI modality is proposed. This study uses FLAIR modality exams and the MNI ICBM 2009a Nonlinear Symmetric atlas in T1 and its white matter mask (WM).

Material e Método / Material and method: The proposed method consists of the following stages: registration of the MNI atlas and its mask within the patient exam; extraction of WM regions in the exam; identification of hyperintensity areas through thresholding using a fixed threshold; and growth of these regions from a variable/adaptive threshold.

Resultados / Results: Tests have been performed in the three first stages so far. Preliminary results show that segmentation is similar to the result obtained by the Lesion Segmentation Tool (LST) of the Statistical Parametric Mapping package, considered the gold standard tool. In quantitative evaluation, a difference was observed in the volume of the lesions. The proposed method obtained a measurement of 4.406ml, against 9.381ml using LST, for the pilot patient. It is expected that the fourth stage of the method will bring lesion measurements closer to the LST results.

Discussão e Conclusões / Discussion and Conclusions: Despite the application of thresholding directed at the WM regions only, the results produced were significantly closer to those expected. The lesion volume encountered, however, was below that obtained by LST. Consequently, bias correction in the exams, refinement of the thresholding process, and implementation of the 4th stage are now required.

Palavras Chave / Key-Words: Multiple sclerosis, brain MRI, FLAIR, automated method, multiple sclerosis lesions

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Passos, G R , Becker, J , Zandoná, M E , Gonçalves, L I , da Silva, A M M , Narciso, L D L , Franco, A , Burger, J L P , Soder, R B , Matushita, C S , Gomes, I

Instituições / Institutions: Instituto do Cérebro do Rio Grande do Sul - PUCRS. - Rio Grande do Sul - Brasil, Serviço de Neurologia, Hospital São Lucas da PUCRS - Rio Grande do Sul - Brasil

Título / Title: Evaluation of microglial activation by PET/CT and association with the appearance of lesions on MRI in patients with relapsing-remitting Multiple Sclerosis

Introdução / Introduction: The application of positron emission tomography scan/computed tomography (PET/CT) labelled with 11C-(R)-PK11195 may have great use in clinical practice as the technique enables alterations to be found in the normal-appearing white matter in disease progression, in addition to being more sensitive than theMagnetic Resonance Imaging(MRI) gadolinium uptake during acute episodes. The objective of this study is to verify the association of microglial activation with clinical (EDSS and MSFC) and radiological data (PET/CT and MRI measures of cortex connectivity and volume) used to assess disease severity.

Material e Método / Material and method: An initial report of the first 8 patients from a project in which a total of 24 relapsing remitting Multiple Sclerosis (RRMS) patients and 5 controls were analysed. The inclusion criteria will be: literate patients, aged between 18 and 60 years, diagnosed with relapsing-remitting MS confirmed by a neurologist according to current criteria proposed by McDonald, revised in 2010. Patients with previously diagnosed psychiatric disorders, with the exception of depression (with appropriate treatment), and those with diseases affecting the central nervous system (CNS) that may interfere with cognitive performance will be excluded. Patients underwent a series of neuropsychological tests, in addition to standard evaluation of disease severity, MRI and PET/CT (labelled with 11C-(R)-PK11195) assessment.

Resultados / Results: Image fusion between the MRI and PET/CT images of the first 8 patients and first 2 controls are presented. Areas of radiotracer retention coincident and non-coincident with the lesions identified in the resonance imaging were observed for the patients with MS.

Discussão e Conclusões / Discussion and Conclusions: Despite the small number of patients, it is believed thatPET/CT(labelled with 11C-(R)-PK11195) can be useful in the diagnosis/monitoring of patients with RRMS.

Palavras Chave / Key-Words: Microglial ativation, PET/CT, brain MRI, relapsing-remitting multiple sclerosis, new lesions

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Forma de Apresentação / Presentation: POSTER

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Instituições / Institutions: Instituto do Cérebro do Rio Grande do Sul - PUCRS - Rio Grande do Sul - Brasil, Serviço de Neurologia, Hospital São Lucas da PUCRS - Rio Grande do Sul - Brasil

Título / Title: Magnetic Resonance Imaging evaluation of brain volume and clinical parameters in Multiple Sclerosis patients

Introdução / Introduction: There is an increasing amount of evidence suggesting the correlation between brain volume loss and physical disability in Multiple Sclerosis (MS) patients. Grey matter atrophy seems to be the most important MRI variable when it comes to development of cognitive impairment, physical disability and prediction of disease progression. Therefore we investigated the clinical implications of different brain volumes measured by MRI, aiming to explore this known correlation among our cohort of MS patients.

Material e Método / Material and method: Preliminary data from 16 relapsing-remitting MS patients either treatment naïve or under treatment with disease-modifying therapies were analyzed. The MRI parameters of brain volume were assessed by means of the Icometrix© software and compared with patients' clinical performances measured by Expanded Disability Status Scale (EDSS) and Multiple Sclerosis Functional Composite (MSFC).

Resultados / Results: A statistically significant correlation of white matter volume and Paced Auditory Serial Addition Test (PASAT) score was observed (R: 0.539 [p=0.031]. A trend to statistical significance was also seen when evaluating grey matter volume and EDSS – inverse correlation (R: -0.490 [p=0.054]) and Timed 25-Foot Walk (T25FW) Z-score– direct correlation (R: 0.0494 [p=0.052]), as when assessing total brain volume and T25FW Z-score and MSFC – both directs correlations (R: 0.462 [p=0.072] and R: 0.432 [p=0.094], respectively).

Discussão e Conclusões / Discussion and Conclusions: MSFC was the clinical parameter that best correlated with total brain and white matter volumes, having T25FW and PASATscores important roles on these associations, respectively. T25FW also seemed to be related with gray matter volume, as did EDSS.The total brain and white matter volumes may probably be affected by the lesion loadand the cortical volume, by the degenerative component, which explain the differences found among related clinical parameters.

Palavras Chave / Key-Words: Brain MRI, multiple sclerosis, brain volume, clinical parameters

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Forma de Apresentação / Presentation: POSTER

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Título / Title: Magnetic Resonance Imaging lesion volume measurements in MS: correlation with clinical parameters

Introdução / Introduction: Magnetic resonance imaging (MRI) has been traditionally used as a tool for the diagnosis and monitoring of Multiple Sclerosis (MS). Several studies attempting to correlate MRI parametric measurementswith patients' physical disability have yielded conflicting results. We aimed, thus, to analyzethe association between MRIlesionsvolumesand subjects'performance in disability scales.

Material e Método / Material and method: We extracted preliminary data from a cohort of 16 relapsing-remitting MS patients, either treatment naïve or under treatment with disease-modifying therapies. Lesion volume was assessed by MRI FLAIR sequence by means of the Icometrix© software, whereas clinical parameters were measured byExpanded Disability Status Scale (EDSS) andMultiple Sclerosis Functional Composite (MSFC).

Resultados / Results: An inverse correlation between lesion volume and the score of 9-Hole Peg Test Z-score was observedamong eligible patients (R: -0.600 [p=0.018]), as was a trend to statistical significance for an inverse correlation with age and MSFC (R: -0.454 [p=0.089] and R: -0.489 [p=0.064], respectively). Correlation involving disease duration, number of relapses, EDSS, 25-Foot Times Walk and Paced Auditory Serial Addition Test (PASAT) did not reach any significance.

Discussão e Conclusões / Discussion and Conclusions: The clinical parameter that best associated with lesion volume was MSFC, mainly to the expense of the 9-Hole Peg Test. Age seemed to be a significant variable as well, but an increased number of subjects may be needed to ratify these findings. Further studies are warranted to confirm these results and to evaluate potential confounders that may contribute to this pattern.

Palavras Chave / Key-Words: Brain MRI, volume measurements, multiple sclerosis, EDSS, MSFC

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Forma de Apresentação / Presentation: POSTER

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Instituições / Institutions: Hospital Geral de Fortaleza - Ceara - Brasil

Título / Title: ANTHROPOMETRIC AND SOCIOECONOMICAL NEUROMYELITIS OPTICA PATIENTS PROFILE IN A REFERENCE CENTRE IN FORTALEZA

Introdução / Introduction: Neuromyelitis Optica (NMO) is a demyelinating, inflammatory and autoimune disease of central nervous system (CNS), whose diagnostic criteria were recently stablished, which makes these patients a poorly characterized population.

Material e Método / Material and method: A descriptive, observational and quantitative study conducted from December 2014 to April 2015, in a Reference Centre for Demyelinating Diseases in Fortaleza - CE, with 57% (17) of the total NMO patients seen (21 women and 9 men). We evaluated: age, time of diagnosis, origin, marital status, education level, current occupation, monthly income, smoking and drinking. The nutritional status was also evaluated: body mass index (BMI) and waist-to-hip ratio (WHR). Data were stored in Microsoft Excel and transferred to SPSS software, version 20.0.

Resultados / Results: The average age was 44 ± 16.5 years and the average time of diagnosis was 4.4 years. Most are from Fortaleza (64.7%; n = 11) and 58.8% are single (n = 10). 41.2% completed a level of higher education (n = 7), while 23.5% have not completed primary school (n = 4) and 58.8% are retired (n = 10). Regarding to family income, the vast majority (88.2%, n = 15) reported receiving 1-3 Brazilian minimum wage. All of them deny smoking and drinking. According to the BMI, overweight is prevalent (47%; n = 8), followed by obesity (29.4%, n = 5) and WHR showed that the majority (70.6%, n = 12) presents cardiovascular risk (CVR).

Discussão e Conclusões / Discussion and Conclusions: Anthropometric parameters indicate overweight and CVR, which combined with increased visceral fat can negatively contribute to the prognosis (OKAUCHI et al, 2007; HAJER; HAEFTEN; VISSEREN, 2008; GOMES et al, 2010). Patients are mostly single, retired, with recent diagnosis, low family income and varying levels of schooling, which could influence the understanding of the disease and level of adherence to treatment.

Palavras Chave / Key-Words: Neuromyelitis optica; Socioeconomic Factors; Anthropometry

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Instituições / Institutions: Hospital Geral de Fortaleza - Ceara - Brasil

Título / Title: Assessment of Fatigue Impact in Multiple Sclerosis Patients Followed up at Reference MS Center in Fortaleza

Introdução / Introduction: Multiple sclerosis (MS) is an inflammatory, chronic, demyelinating disease that affects young adults in their most productive time of life. One of the most common clinical manifestation is fatigue, defined as a subjective sensation of decreased energy, physical or mental, and these symptoms often generate a direct and negative impact on quality of life. The aim of this study was to evaluate the impact of fatigue in patients with multiple sclerosis in Fortaleza General Hospital (FGH).

Material e Método / Material and method: It is a cross-sectional, prospective study with a quantitative approach developed at the Clinic of demyelinating diseases at FGH. The sample consisted of 35 patients followed up in the period of February to June, 2015. Data were collected from the physical therapy assessment form and from the Modified Fatigue Impact Scale (MFIS-BR). The impact of fatigue was categorized into no impact (MFS <38), low impact (MFIS between 39 and 58) and high impact (MFIS> 59). This study complied with Resolution 466/12 of the National Health Council.

Resultados / Results: It was observed that 85.7% (n = 30) were female, with a mean age of 37.49 years old (sd 12.71). With regard to the prevalent age group, 31.4% (n = 11) are between 20-27 years old, 20% (n = 7) between 28-35 years old, 17.1% (n = 6) between 36-43 and 17.1% (n = 6) between 44 to 51 years old. Fatigue was observed in 51.4% (n = 18), of these, 14 were female. Concerning the impact of fatigue, 48.6% (n= 17) had no impact, 34.3% (n = 12) low impact and 17.1% (n = 6) high impact. There were no statistically significant correlations between sex, age and the level of fatigue ($p<0.005$)

Discussão e Conclusões / Discussion and Conclusions: We conclude that although fatigue is a common finding in MS patients, it didn't have significant impact on the performance of daily living activities in this study group at our hospital. However, we should continue this study to observe a higher number of patients.

Palavras Chave / Key-Words: Multiple Sclerosis; Fatigue; Quality of Life

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Instituições / Institutions: Hospital Geral de Fortaleza - Ceara - Brasil

Título / Title: Urinary Dysfunction among Women with Demyelinating Diseases Followed up at Fortaleza General Hospital - a Reference Center in Ceara

Introdução / Introduction: Demyelinating diseases result in functional limitations that can lead to various disabilities, among them urinary dysfunction, which generates great social impact (professional, sexual, psychological and economic) negatively affecting the quality of life of these patients. The aim of this study was characterize urinary dysfunction in women with demyelinating diseases.

Material e Método / Material and method: The study population was composed by women with demyelinating diseases followed up at the neurology clinic of Fortaleza General Hospital – FGH between April and June 2015. Data were collected through the physical therapy assessment form that addresses issues of the neurological disease and urinary disorders. This study complied with Resolution 466/12 of the National Health Council. Data were statistically analyzed using SPSS version 18.0.

Resultados / Results: In total, 57 women were interviewed, of which 71% (n = 41) showed some urinary dysfunction. In this group, 70.7% (n = 29) had Multiple Sclerosis, 17.1% (n = 7) neuromyelitis optica, 7.3% (n = 3) Transverse Myelitis, 2.4% (n = 1) Clinical Isolated Syndrome and 2.4% (n = 1) other. The average age was 37 years old, with a minimum age of 19 and maximum of 62 years. With regard to urinary dysfunction, nocturia was reported by 67.5% (n = 27) patients, followed by urgency 51.2% (n = 21), Frequency increased 48.8% (n = 20), urinary retention 34.1% (n = 14), urge incontinence 31.7% (n = 13) and 17.5% (n = 7) were losing urine unintentionally.

Discussão e Conclusões / Discussion and Conclusions: Most of the interviewed patients showed some urinary dysfunction, possibly also affecting their quality of life. It emphasizes the importance of guidance and treatment of these disorders according to the guidelines of the International Continence Society (ICS).

Palavras Chave / Key-Words: Demyelinating diseases, urinary incontinence, quality of life.

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Forma de Apresentação / Presentation: POSTER

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Instituições / Institutions: Hospital de Base do Distrito Federal - Distrito Federal - Brasil

Título / Title: Analysis of epidemiological data from NMO and NMOSD patients accompanied at the Hospital de Base - Distrito Federal - Brazil (2001-2015)

Introdução / Introduction: Neuromyelitis Optica (NMO), or Devic's disease, is an autoimmune inflammatory disorder characterized by severe optic neuritis and extensive transverse myelitis, as described in Wingerchuk diagnostic criteria. NMO spectrum disorder (NMOSD) is a more comprehensive definition, recently proposed to include the restricted forms of the disorder: optic neuritis or tranverse myelitis recurrent or brain injury symptoms related to periventricular areas, associated with or without anti-aquaporina 4 (anti-AQP4) positive. The aim of this work is to describe a series of patients diagnosed with NMO or NMOSD and accompanied in regular outpatient visits.

Material e Método / Material and method: We retrospectively assessed the medical records of all patients diagnosed with NMO or NMOSD from 2001 to 2015. We collected epidemiological and clinical data to describe their profile and outcomes.

Resultados / Results: Twenty two patients fulfilled the diagnostic criteria. This resulted in 111,1 patients-years of follow-up. Nineteen (86.4%) were female, the mean age of the series was 40.9±2.7 yo, ranging from 21 to 67 years. Anti-AQP4 was positive in 68.2% of patients, and was still not tested in 4.5%. The mean time of disease in the sample was 60.6±8.8 mo. The average time from the onset of symptoms until diagnosis was 22.7±6.3 mo. Fourteen (63.6%) patients are in use of azathioprine, seven (31.8%) are in use of rituximab, and 4.5% are without treatment due to a recently diagnosed pregnancy. Two deaths were observed, one in 2014 and other in 2015 that resulted in a mortality rate of 9.1%.

Discussão e Conclusões / Discussion and Conclusions: NMO and NMOSD are disabling diseases, with a high mortality. Our data are in agreement with the literature, showing a higher proportion of women in the case series. There are still delays in the diagnosis and the start of treatment. And the clinical criteria need to be revised to decrease this delay.

Palavras Chave / Key-Words: Neuromyelitis óptica; Devic's desease; NMO spectrum

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Forma de Apresentação / Presentation: POSTER

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Instituições / Institutions: Multimagem Santos - Sao Paulo - Brasil, Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Brain volume in multiple sclerosis: is this the way ahead?

Introdução / Introduction: Measurements of brain volume in patients with multiple sclerosis (MS) have recently yielded a variety of interesting papers in the literature. The subject is new, challenging and will possibly grow to occupy significant space in MS research. The objective of the present study is to review the main aspects of brain volume in MS.

Material e Método / Material and method: This is a comprehensive literature review of brain volume, presenting aspects of white and grey matter atrophy in patients with MS. Regional atrophy is also discussed.

Resultados / Results: Although the initial reports on accelerated brain atrophy in patients with MS date from the 70s, it is only recently that means to evaluate this tissue loss have become available. There is a variety of programs for assessing whole and regional brain volumes, as well as lesion load. The most used software programs are SIENA, SIENAX, lesion-TOADS, Brain Parenchimal Fraction (BPF), and NeuroQuant. The established cut-off point of accepted normal brain “shrinkage” is 0.4% per year for adults, at least for European and North American populations (so far the only ones reported in the literature). In MS, not only corpus callosum, ventricles and white matter have their shape changed over the years, but also deep gray matter areas are involved in this accelerated atrophy process. Thalamus and basal ganglia are particularly affected in patients with MS who have more severe cognitive dysfunction.

Discussão e Conclusões / Discussion and Conclusions: Although still in its early stages, correlation of brain atrophy (regional and global) with mental and physical disability seems to be on its way to become an important aspect of MS research. Brain volume may become a potential outcome measurement for clinical trials.

Palavras Chave / Key-Words: brain; atrophy; multiple sclerosis; magnetic resonance

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Brooks, J B B , Oliveira, C L S , Fragoso, Y D

Instituições / Institutions: Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Fabry disease misdiagnosed as multiple sclerosis: a case report.

Introdução / Introduction: Fabry's disease is recessive X-linked lysosomal storage disorder resulting from abnormal deposits of globotriaosylceramide (Gb3, or GL-3). Signs and symptoms of the disease typically appear in adults and the disease takes a long course before diagnosis is established. Exclusive neurological progressive forms of Fabry disease are particularly rare and may be confounded with multiple sclerosis (MS).

Material e Método / Material and method: case report

Resultados / Results: In 2013, a 33-year-old female was referred to CEREM Litoral Paulista with the diagnosis of primary progressive multiple sclerosis. In 2006, she complained of an insidious and progressive left appendicular incoordination. In 2009, she had a second attack, with dysarthria, dysphagia, tetraparesia, decreased level of consciousness and generalized tonic clonic seizures. During this second attack, she was hospitalized and the analysis of cerebrospinal fluid, hematological tests, and urinalysis were all normal. Cerebral MRI examination showed large confluent lesions of the white matter. Brain biopsy was also performed but no pathological pattern was confirmed. Four years later, she was complaining of bilateral reduction of auditory acuity and chronic diarrhea. She was chair bound, with tetraparesia with pyramidal signs and cerebellum involvement. When asked, she mentioned an episode of deep venous thrombosis in her left leg in 2001, and informed us of her father's death at the age of 32 years, due to acute myocardial infarction. Her cerebral MRI in 2013 (suggested the possibility of Fabry disease. This diagnosis was confirmed genetically by Exon 2-p.R118C heterozygosis. The patient has started treatment ad in six months progressed to ambulation with support. No involvement of kidney or skin could be detected at any time

Discussão e Conclusões / Discussion and Conclusions: The patients did not have other manifestations of Fabry's disease. This points out to the need of screening for Fabry in atypical cases of MS.

Palavras Chave / Key-Words: Fabry; multiple sclerosis; magnetic resonance

Immunology, basic science and clinical findings

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Instituições / Institutions: Universidade Estadual de Londrina - Parana - Brasil

Título / Title: Ferritin, albumin, and oxidative stress biomarkers predict multiple sclerosis and its clinical forms

Introdução / Introduction: The aim of the present study was to evaluate inflammatory and oxidative stress blood biomarkers as possible predictors of MS and its clinical forms.

Material e Método / Material and method: This study included 258 MS patients [175 with relapsing-remitting MS (RRMS) and 83 with progressive MS clinical forms] and 249 healthy individuals. Peripheral blood samples were obtained to determine serum levels of inflammatory and oxidative stress biomarkers.

Resultados / Results: MS patients showed higher ferritin (p<0.001) and lipid hydroperoxide (p<0.001), and lower albumin (p=0.001), total antioxidant capacity evaluated by total radical-trapping antioxidant parameter (TRAP, p=<0.001), advanced oxidation protein products (AOPP, p=0.013) and nitric oxide metabolites (NOx, p=<0.001) than controls. Difference was not observed in C-reactive protein (CRP), total protein or carbonyl proteins between MS patients and controls. Ferritin (OR: 1.006; 95% CI: 1.003-1.009, p<0.001) and lipid hydroperoxide (OR: 1.029, 95% CI: 1.007-1.052, p=0.009) showed positive association with MS. Albumin (OR: 0.309, 95% CI: 0.116-0.824, p=0.019), TRAP (OR: 0.996, 95% CI:0.993-0.999, p=0.003), AOPP (OR: 0.989, 95% CI: 0.982-0.995, p=0.001), and NOx (OR: 0.980, 95% CI: 0.967-0.993, p=0.003) were negatively associated with MS. Using this regression analysis, 82.7% of all subjects were correctly classified with a sensitivity of 73.6% and a specificity of 89.5%. MS patients with progressive forms showed lower albumin (OR: 0.155, 95% CI=0.032-0.756, p=0.012) and higher AOPP (OR: 1.011, 95% CI=1.001-1.021, p=0.037) than RRMS.

Discussão e Conclusões / Discussion and Conclusions: Taken together, the results showed that ferritin, albumin, and oxidative stress biomarkers may be considered good predictors of MS and AOPP and albumin may contribute to differentiate the clinical forms of the disease.

Palavras Chave / Key-Words: ferritin, multiple sclerosis, oxidative stress, ferritin

Código / ID: PL 009

Data / Date: 2015-08-20

Horário / Time: 17:00:00 às 17:15:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: PLATFORM

Autores / Authors: Kallaur, A P , Oliveira, S R , Simão, A N C , Lozovoy, M A B , Pereira, W L , Alfieri, D F , Flauzino, T , Amorin, B L , Moura, L A d , Proença, C d M , Kaimen-Maciel, D R , Maes, M , Reiche, E M V

Instituições / Institutions: Universidade Estadual de Londrina - Parana - Brasil

Título / Title: Genetic, inflammatory, and oxidative stress markers as potential predictors for the susceptibility to multiple sclerosis and progression of disability

Introdução / Introduction: To evaluate the TNFβ NcoI polymorphism (rs909253), inflammatory, and oxidative stress markers as potential predictors for susceptibility to MS, disability, and disease progression.

Material e Método / Material and method: MS patients (n=212) and healthy controls (n=249) were included. MS patients were divided in two groups (EDSS < 3 and EDSS ≥ 3) TNFβ NcoI polymorphism was determined using PCR-RFPL.Serum levels of cytokines, oxidative stress markers were evaluate

Resultados / Results: The TNFB2 allele was higher in MS patients than in controls; IL-10, TNFα, and IFN-gamma were higher and IL-4 was lower in MS patients with EDSS ≥ 3 than those with EDSS < 3. Higher CL-LOOH was obtained in the two MS groups than in controls, AOPP was lower in those with EDSS < 3 than in controls and MS patients with EDSS ≥ 3, NOx was lower in the two MS groups than in controls and lower in those with EDSS <3 than those with EDSS ≥ 3. Ferritin was higher in the two MS groups than controls. EDSS was an independent factor associated with the clinical course and progression of disability. Univariate GLM analysis showed that 38.4% of the variance in the 2011 EDSS was explained by age (positively associated), CL-LOOH (positively associated), drugs and the interaction term relapsing remitting MS with drugs. In subjects without the TNFB1/B2 genotype there was a higher increase in EDSS in pyramidal symptoms from 2006 to 2011 than in those with the TNFB1/B2 genotype. The results also showed that 9.6% of the variance in the endpoint pyramidal symptoms were explained by increasing age and IFN-gamma levels

Discussão e Conclusões / Discussion and Conclusions: This study showed a model of potential markers that may be used as predictors for the susceptibility to MS and disability. While TNFβ rs909253 polymorphism, oxidative stress, and ferritin were good predictors for MS, low IL-4 and high IL-10, TNF-α, IFN, AOPP, and NOx may predict high disability in MS patients.

Palavras Chave / Key-Words: multiple sclerosis, disability, TNFβ NcoI polymorphism, cytokines, oxidative stress, pyramidal symptoms.

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Data / Date: 2015-08-20

Horário / Time: 17:15:00 às 17:30:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: PLATFORM

Autores / Authors: Oliveira, S R , Reiche, E M V , Kallaur, A P , Morimoto, H K , Pereira, W L , Nagata, K S , Grotti, D M , Martins, G G , Proença, C d M , Sabino, B S , Alfieri, D F , Flauzino, T , Kaimen-Maciel, D R , Simão, A N C

Instituições / Institutions: Universidade Estadual de Londrina - Parana - Brasil

Título / Title: VITAMIN D IS ASSOCIATED WITH OXIDATIVE STRESS MARKERS AND DISABILITY IN MULTIPLE SCLEROSIS PATIENTS

Introdução / Introduction: The aim of this study was to assess whether low serum levels of vitamin D were associated with oxidative stress markers and with progression of disease in MS patients.

Material e Método / Material and method: This study included 137 MS patients and 218 controls. Blood samples were obtained to evaluate 25(OH) vitamin D and OE markers, such as lipid hydroperoxides, advanced oxidation protein products (AOPP), total antioxidant capacity using the total radical-trapping antioxidant parameter (TRAP), and nitric oxide metabolites (NOx). The oxidative stress index (OSI) was also determined. MS patients were divided in two groups: 25(OH) vitamin D ≥30 ng/mL and <30 ng/mL

Resultados / Results: MS patients presented higher age ($p<0.0001$) and OSI ($p=0.028$) and lower 25(OH) vitamin D ($p=0.0004$), TRAP ($p=0.024$), and NOx ($p<0.0001$) than controls. When the age was used as an additional explanatory variable in logistic regression analyses, only 25(OH) vitamin D and NOx remained significant. Patients with 25(OH) vitamin D <30 ng/mL showed higher EDSS score ($p=0.048$), lipid hydroperoxides ($p=0.037$), and AOPP ($p=0.017$) than those with ≥ 30 ng/mL. A negative correlation was observed between 25(OH) vitamin D and EDSS ($r=-0.311$; $p=0.038$). The linear regression analysis demonstrated that 25(OH) vitamin D and age of MS patients may explain 20.6% of the EDSS variation ($R2 =0.206$, $p=0.007$). Moreover, patients with RRMS showed higher 25(OH) vitamin D than those with progressive forms ($p=0.024$). However, after age and ethnicity adjusted, 25(OH) vitamin D did not remain significant, suggesting an interference of these two variables in the levels of this hormone.

Discussão e Conclusões / Discussion and Conclusions: These results suggest that low levels of vitamin D and age are predictors of disability independently of the MS clinical forms and are associated with increased oxidative stress markers in this population.

Palavras Chave / Key-Words: Vitamin D, EDSS, disability, oxidative stress

Código / ID: PO 012

Data / Date: 2015-08-21

Horário / Time: 16:30:00 às 18:00:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: POSTER

Autores / Authors: LIMA, F P , SOUSA, A R A , VIANA, A T , ARAÚJO, M P , MELO NETO, A P , MORAIS, A A , TAVARES, J W L , GONDIM, F A A

Instituições / Institutions: Universidade Federal do Ceará - Ceara - Brasil

Título / Title: Good Outcome After Untreated Herpes Zoster Secondary To Treatment With Fingolimod

Introdução / Introduction: With the advent of newer treatments for Multiple Sclerosis (MS), such as fingolimod, natalizumab an alemtuzumab, zoster infections caused by varicella-zoster virus (VZV) became more common.

Material e Método / Material and method: A 48-year old woman, diagnosed with MS in 2008, after an episode of lower limb paresthesias and band-like pattern of pain around the umbilical area. She later developed ataxia, horizontal and vertical nystagmus, lower limb sensory loss and hyperreflexia. Her Brain MRI revealed advanced disease, with multiple scattered lesions and atrophy and MRIs of the cervical spine also revealed evidence of myelitis. She was treated with Betaferon, Rebif and Copaxone until 2014. On March 2014, due to therapeutical failure, Fingolimod was started. After 3 months of treatment, she developed signs of skin rash from L5 to S1, on the left side. After 14 days without treatment, the patient was diagnosed with herpes zoster.

Resultados / Results: The treatment with acyclovir was recommended, but the patient did not follow our recommendations and subsequently developed superimposed bacterial skin infections, that was successfully treated with cephalexin. Two months after the treatment of bacterial skin infection, she had no signs of postherpetic neuralgia.

Discussão e Conclusões / Discussion and Conclusions: Our patient shows that zoster cases after treatment of multiple sclerosis can be mild and with a favorable outcome even without adequate treatment with acyclovir.

Palavras Chave / Key-Words: Multiple Sclerosis, Herpes Zoster, Varicella-Zoster Virus, Fingolimod.

Código / ID: PO 013

Data / Date: 2015-08-21

Horário / Time: 16:30:00 às 18:00:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: POSTER

Autores / Authors: Pitombeira, M S , Melo, M L P d , Lima, A C , Morais, K R F d , Martins, G J , D'Almeida, P C R , D'Almeida, J A C

Instituições / Institutions: Hospital Geral de Fortaleza - Ceara - Brasil

Título / Title: Multiple sclerosis and Ankylosing spondylitis in an HLA-B27 negative patient: How to treat?

Introdução / Introduction: The association between multiple sclerosis (MS) and ankylosing spondylitis (AS) has been reported sporadically in the literature and, also treatment options in coexistence of both.

Material e Método / Material and method: We report a case of coexistence of MS and AS and review the possible pathophysiology and treatment options available in the literature.

Resultados / Results: A 25-year-old woman presented with optic neuritis in the left eye. MRI fulfilled McDonald´s criteria for MS and CSF showed oligoclonal bands. Then, beta interferon 1a was started. In the last 3 years, the patient complained about low back pain that improved with activity, with worsening of symptoms after the diagnosis of MS. MRI of the sacroiliac joints showed bilateral sacroiliitis , which together with symptoms met the modified NY criteria for AS. HLA-B27 was negative.

Discussão e Conclusões / Discussion and Conclusions: Although both diseases have not fully understood pathophysiology, mechanisms based on autoimmunity mediated by T-cells and association with certain HLA antigens are some of the points shared between MS and AS. Until 2004, only one case of these two diseases had been reported in a negative HLA-B27 patient. In a study published in 2008, of the 21 patients with spondyloarthropathy and MS, 17 met the criteria for AS and only 3 had negative HLA-B27. Due to the rarity of coexistence, management of these patients becomes a challenge and recent studies have associated the use of anti TNF-alpha with demyelinating diseases similar to MS. Other therapies for MS are contradictory for AS (beta interferon), have insufficient data (glatiramer acetate, azathioprine, natalizumab, fingolimod) or its efficacy in MS/AS is associated with a higher risk treatment (rituximab). Further studies are needed to make a definitive conclusion on the association between MS and EA. However, it is necessary to discuss the treatment options in these patients, since the two conditions have potential to generate serious disabilities in medium and long term.

Palavras Chave / Key-Words: Multiple Sclerosis; ankylosing spondylitis;

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Data / Date: 2015-08-21

Horário / Time: 16:30:00 às 18:00:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: POSTER

Autores / Authors: GRIPPE, T C , Aguilar, A C R , Martins, H N F , Sousa, M W G , da Costa, N S C , Barbosa, A L , Carneiro, N M , Barzilai, C C R M , Gigante, R L G , de Maria, P R S , Aguiar, M S , Tauil, C B

Instituições / Institutions: HOSPITAL DE BASE DO DISTRITO FEDERAL - Distrito Federal - Brasil

Título / Title: Herpes reactivation after Fingolimod: Should we stop the treatment?

Introdução / Introduction: Fingolimod is a selective immunossupressor, which holds T cells in lymph nodes, leading to reduced numbers of peripheral blood lymphocytes. It did not lead to increased rates of severe infection in clinical phase 3 studies. However, immunity against herpes viruses showed subtle impairments in these patients. Since then, vaccination is recommended for VZV-seronegative patients prior to the initiation of fingolimod. We describe three cases of herpes virus reactivation despite a positive baseline serology.

Material e Método / Material and method: Description of three cases and comparison with previous published data, in order to discuss the efficiency and indication of herpes virus vaccine in patients using fingolimod.

Resultados / Results: Case 1: Female, 19 y.o., with relapsing-remitting multiple sclerosis (RR – MS) since 2012, with multiple demyelinating lesions, urinary incontinence, sensory syndrome, anxiety and fatigue. Baseline EDSS: 2.0. Treated with steroids, IFN-beta, glatiramer acetate and started fingolimod 16 months ago due to therapeutic failure. After eight months, she developed recurrent genital herpes. Positive baseline IgG for herpes.Case 2: Female, 31 y.o., RR-MS since 2012, multiple demyelinating lesions and needle phobia. Baseline EDSS: 2.0. Treated with steroids and fingolimod, due to agressive MS. After 2 years of fingolimod, developed a palate HSV activation. Baseline positive IgG for herpes.

Discussão e Conclusões / Discussion and Conclusions: There is no established consensus about changing the treatment after the infection and the possible effects. It was already described a rebound of MS after the intracranial reactivation of VZV and fingolimod withdrawal, due to restoration of CNS immune surveillance. Moreover, it was showed that the vaccine during use of fingolimod may increase the risk of viral shedding and have a reduce efficacy, reinforcing that this drug interaction with herpes virus is not well understood and should be more explored in order to decide about it future uses.

Palavras Chave / Key-Words: Fingolimod, Herpes virus, vaccination

MS treatment and multidisciplinary care

Código / ID: PL 001

Data / Date: 2015-08-20

Horário / Time: 14:30:00 às 14:45:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: PLATFORM

Autores / Authors: da Fonseca, B A , Pereira, C B , Jorge, F M H , Simm, R , Apóstolos-Pereira, S , Callegaro, D

Instituições / Institutions: University of São Paulo Medical School - Sao Paulo - Brasil

Título / Title: Failure of motor learning associated with balance disorders in people with multiple sclerosis

Introdução / Introduction: Control of posture and movement uses anticipatory and reactive mechanisms, both of which are modulated by sensory input and influenced by learning and experience. These adjustments are modulated with environmental context and learned with repetition. A hallmark of motor learning is a gradual reduction in errors over repeated trials in the novel environment. Since postural balance disorders is a characteristic symptom in patients with multiple sclerosis (PwMS), our aim was to determine the learning effect with repetitive balance tests.

Material e Método / Material and method: We evaluated 70 PWMS (EDSS 0 – 4.0). They were divided into two groups according to their self-report about balance problem: without balance problem (w/oBP, n=38) and with balance problem (wBP,n=32). We excluded patients with other neurological diseases, dizziness, cognitive and visual impairment. Balance was tested with the Computerized Dynamic Posturography (NeuroCom). SOT consists of 3 repetitions for 4 sensory conditions. Postural balance sway was recorded during each trial. Binomial test was used to analyze data.

Resultados / Results: Motor learning effect was different between groups during conditions with somatosensory reduction (conditions 3 and 4, when subjects were required to maintain balance control on unstable surface). The w/oBP group have learned the task, reducing the sway area after repetitions, while wBP group did not ($p<0,01$)

Discussão e Conclusões / Discussion and Conclusions: It has been reported that repeated exposure to a given perturbation of the postural control system allows for motor learning of more efficient postural strategies to maintain balance within a session. Similar to previous studies with healthy controls, patients without balance problems showed greater learning in more complex tasks, since improved their balance strategies. Nevertheless, in those who complained about balance problem we found the inability to learn and adapt postural balance during more complex environment context.

Palavras Chave / Key-Words: Multiple sclerosis, postural balance, motor learning, postural adjustments, posturography.

Código / ID: PL 011

Data / Date: 2015-08-20

Horário / Time: 17:30:00 às 17:45:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: PLATFORM

Autores / Authors: Fragoso, Y D , Gomes, S , Goncalves, M V M , Machado, S C N , Morales, R R , Oliveira, F T M , Olmo, N R S , Parolin, M K F , Siquineli, F , Stoney, P N

Instituições / Institutions: Centro Hospitalar Unimed, Joinville - Santa Catarina - Brasil, Hospital Beneficencia Portuguesa and Hospital Paulistano, Sao Paulo - Sao Paulo - Brasil, Imperial Hospital de Caridade, Hospital Governador Celso Ramos. Florianopolis - Santa Catarina - Brasil, Neurologic Clinic Curitiba, Curitiba - Parana - Brasil, Universidade Federal de Uberlandia, Uberlandia - Minas Gerais - Brasil, Universidade Metropolitana de Santos, Santos - Santa Catarina - Brasil, Universidade Regional de Blumenau, Blumenau - Santa Catarina - Brasil, University of Aberdeen, Aberdeen - - Grã-Bretanha (Reino Unido)

Título / Title: Patients with multiple sclerosis do not necessarily consume more alcohol, tobacco and illicit drugs than the general population

Introdução / Introduction: Although not a well-explored subject, the literature on patients affected by multiple sclerosis (MS) abusing of alcohol, tobacco and illicit substances is consistent. However, this was not the impression of many neurologists in Brazil and the present study was designed to assess this matter.

Material e Método / Material and method: Patients with MS and matched control subjects were assessed in a cross-sectional, transversal manner. Validated questionnaires on depression, anxiety, socioeconomic level, use of alcohol, tobacco and illicit drugs were applied individually.

Resultados / Results: A total group of 168 patients and 168 control subjects were assessed. There were no significant differences in the use of tobacco and illicit drugs between patients with MS and controls. However, when the use of alcohol was assessed, control subjects scored significantly higher values on the AUDIT scale ($p = 0.0001$) than did patients with MS. Regarding smoking, 23.3% of control subjects had a past or present history of cigarette smoking, with an average of 12 cigarettes per day. Patients with MS had a similar past or present history of cigarette smoking (24.5%), but an average of only five cigarettes per day. The illicit drugs used by the patients and controls included cocaine, crack, marijuana, amphetamine, inhalers, hypnotic, sedative, hallucinogenic and opioid drugs, all without medical prescription. Previous or present use of illicit drugs was found in 13.1% of the patients with MS and 15.6% of the controls.

Discussão e Conclusões / Discussion and Conclusions: The present study did not confirm the findings of misuse of alcohol, tobacco or illicit drugs by patients with MS. In fact, the control subjects made higher use of alcohol than did the patients and, when asked about alcohol during our interviews, many patients mentioned that “you are not supposed to drink if you have MS”. It is possible that the results obtained in Brazil represent a cultural attitude towards dis

Palavras Chave / Key-Words: multiple sclerosis; alcohol; tobacco; illicit drugs; anxiety; depression

Código / ID: PL 012

Data / Date: 2015-08-20 | **Horário / Time:** 17:45:00 às 18:00:00

Sala / Room: Auditorium | **Forma de Apresentação / Presentation:** PLATFORM

Autores / Authors: Fragoso, Y D , Adoni, T , Ales-Leon, S V , Apostolos-Pereira, S L , Araujo, Y R , Becker, J , Brooks, J B B , Correa, E C , Damasceno, A , Damasceno, C A A , Ferreira, M L B , Gama, P D , Gama, R A D , Gomes, S , Gonçalves, M V M , Grzesiuk, A K , Machado, S C N , Matta, A P d C , Mendes, M F , Ribeiro, T A G J , Rocha, C F , Ruocco, H H , Sato, H , Simm, R F , Tauil, C B , Vasconcelos, C C F , Vieira, V L F

Instituições / Institutions: Centro de Reabilitação Integral Dom Aquino Correa - Mato Grosso - Brasil, Centro Hospitalar Unimed - Santa Catarina - Brasil, Department of Neurology, CLINEN, Brasilia - Distrito Federal - Brasil, Faculdade de Medicina de Jundiai - Sao Paulo - Brasil, Hospital Beneficencia Portuguesa de Sao Paulo - Sao Paulo - Brasil, Hospital da Restauração - Pernambuco - Brasil, Hospital das Clinicas da Universidade de Sao Paulo - Sao Paulo - Brasil, Hospital de Base do Distrito Federal - Distrito Federal - Brasil, Hospital de Caridade, Florianopolis - Santa Catarina - Brasil, Hospital Sirio Libanes - Sao Paulo - Brasil, Institute of Neurology, Curitiba - Parana - Brasil, Irmandade da Santa Casa de Misericordia de Sao Paulo - Sao Paulo - Brasil, Neurological Clinic Belo Horizonte - Minas Gerais - Brasil, Pontificia Universidade Catolica do Rio Grande do Sul - Rio Grande do Sul - Brasil, Pontificia Universidade Catolica Sorocaba - Sao Paulo - Brasil, Universidade Estadual de Campinas - Sao Paulo - Brasil, Universidade Fedearl do Espirito Santo - Espirito Santo - Brasil, Universidade Federal de Goias - Goias - Brasil, Universidade Federal de Juiz de Fora - Minas Gerais - Brasil, Universidade Federal do Estado do Rio de Janeiro - Rio de Janeiro - Brasil, Universidade Federal do Rio de Janeiro - Rio de Janeiro - Brasil, Universidade Federal Fluminense - Rio de Janeiro - Brasil, Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Reduced risk of relapses in the switch between natalizumab and fingolimod in 96 patients

Introdução / Introduction: Natalizumab (NTZ) is a good therapeutic option for patients with multiple sclerosis (MS), particularly those with very aggressive disease. However, long-term use of NTZ increases the risk of developing progressive multifocal leukoencephalopathy (PML), a potentially fatal disease. Withdrawal of NTZ may be necessary in order to minimise the risks of PML, but acute reactivation of MS has been described as a frequent complication of NTZ withdrawal. Most researchers have concerns regarding the safety of an early switch to fingolimod (FTY) after NTZ withdrawal and recommend a long washout period between the two drugs. Consequently, the risk of disease reactivation when FTY is started after the washout is high. The present study presents alternatives for the washout period that lead to reduced incidence of relapses.

Material e Método / Material and method: This was na open prospective observational study. Data were collected on 96 patients. Each participating physician took his/her own decision on how to proceed with the drug switch, according to his/her best judgment, considering that there were no specific guidelines to follow. The alternatives were “no washout” (switch to FTY done 4 to 8 weeks after NTZ withdrawal) or “corticosteroids during washout” (monthly pulses of methylprednisolone (MP) 1 g per day, for 3 days until starting FTY).

Resultados / Results: Thirty-seven patients had no washout period, while all others used monthly pulses of MP for 3 to 12 months between drugs. The median follow-up period was 6 months (range: 3 to 27 months). Relapse rate was 11%.Regarding adverse events (other than relapses), there were five cases of headache, two of lymphopenia and two of increased hepatic enzymes. There were no significant changes in these patients’ degree of disability, as assessed using EDSS.

Discussão e Conclusões / Discussion and Conclusions: This is the lowest relapse rate reported in the literature when NTZ is swithced to FTY.

Palavras Chave / Key-Words: multiple sclerosis; relapses; natalizumab; fingolimod

Código / ID: PL 013

Data / Date: 2015-08-20

Horário / Time: 18:00:00 às 18:15:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: PLATFORM

Autores / Authors: Fragoso, Y D , Gama, P D , Adoni, T , Brooks, J B B , Ferreira, M L B , Gama, R A D , Gonçalves, M V M , Matta, A P d C , Parolin, M K F

Instituições / Institutions: , Hospital da Restauracao - Pernambuco - Brasil, Hospital Sirio Libanes - Sao Paulo - Brasil, Neurology Unit, Fundacao Unimed - Santa Catarina - Brasil, Neurology Unit, State Health Department, Curitiba - Parana - Brasil, Pontificia Universidade Catolica de Sao Paulo, Campus Sorocaba - Sao Paulo - Brasil, Universidade Federal Fluminense - Rio de Janeiro - Brasil, Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: The evidence-based checklist for optimal disease control in multiple sclerosis

Introdução / Introduction: The therapeutic options for managing multiple sclerosis (MS) are expanding. The correct moment for switching between two drugs is of critical importance, since the only reason for this therapeutic strategy is an observed suboptimal response to a given treatment. Although "therapeutic failure" is the recommended reason for drug switch in all guidelines, the definition of "therapeutic failure" is not clear and, in fact, the expression is inadequate.

Material e Método / Material and method: Following on from an extensive review of the literature and a meeting of experts, the present paper was designed to provide a checklist of items of relevance to discussing whether MS is indeed under optimal control.

Resultados / Results: Adherence to treatment, modification of life habits, adverse events, relapse rate, magnetic resonance imaging (MRI), disability, cognition and retinal nerve fiber layer thickness were all discussed in detail. The aim of MS treatment is to achieve optimal disease control. The degree of control needs to be assessed regularly by the neurologist, through comprehensive evaluation of clinical signs and symptoms (to identify adherence to treatment, adverse events, relapses and disability progression) and imaging findings (new lesions on MRI) after 12 months of treatment. Cognitive worsening and OCT findings do not justify drug switch at present. Clinical relapses, two or more new lesions in T2 and EDSS increment of at least 1.0 point are indicative of subotpimal response.

Discussão e Conclusões / Discussion and Conclusions: A practical checklist for guiding the diagnosis of suboptimal response and the need for drug switching was created from data in the literature. Although ultimately a decision of the doctor and the patient, switching between drugs should be performed in cases of suboptimal response.

Palavras Chave / Key-Words: multiple sclerosis; therapeutic failure; adherence; adverse events; relapses.

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Horário / Time: 18:15:00 às 18:30:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: PLATFORM

Autores / Authors: Fragoso, Y D

Instituições / Institutions: Neuroimmunology Angiocorpore - Sao Paulo - Brasil, Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Vitamin D does not cure all ailments and evils.

Introdução / Introduction: Low plasma levels of vitamin D have been associated with a large number of diseases, many of which have nothing in common. In neurology, multiple sclerosis (MS) has been the focus of many papers on the possible associations between vitamin D insufficiency and disease development, activity and progression. Without any evidence, vitamin D has been proclaimed to be the cure for MS and some patients have abandoned all conventional treatments in order to submit themselves to vitamin D therapeutic protocols.

Material e Método / Material and method: Comprehensive review of the literature on the subject of vitamin D and MS.

Resultados / Results: At present, it cannot be established whether low plasma levels of vitamin D and chronic diseases truly represent an association, a causative relationship, a consequence, or all of these. While one systematic review showed that this supplementation might have a positive effect on preventing death, other authors showed the flaws in that review and concluded that no effect on mortality could be seen through supplementation with vitamin D. There is no evidence that vitamin D supplementation is efficient and safe for prevention of cancer. Low levels of vitamin D are not associated with rheumatoid arthritis. The relationship between obesity and low vitamin D levels has now been shown to be a consequence of obesity itself.

Discussão e Conclusões / Discussion and Conclusions: There is no doubt that vitamin D is an important factor for immune homeostasis, through modulating various immune cells (monocytes, macrophages, dendritic cells, T-lymphocytes and B-lymphocytes). However, there is no evidence-based recommendation for including vitamin D (particularly in high doses) in the treatment of MS. In fact, For diseases like MS, treatment with vitamin D is, at present, only a concept.

Palavras Chave / Key-Words: multiple sclerosis; vitamin D; immunology

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Data / Date: 2015-08-21

Horário / Time: 16:30:00 às 18:00:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: POSTER

Autores / Authors: Aguilar, A C R , Grippe, T C , Tauil, C B , Maciel, R , Sousa, M W , Martins, H N , Gigante, R L , Carneiro, N M , Barbosa, A L , Ferreira, M A

Instituições / Institutions: Hospital de Base do Distrito Federal - Distrito Federal - Brasil

Título / Title: Clinical Experience with Natalizumab Treatment in Multiple Sclerosis: Report of a Case Series

Introdução / Introduction: Natalizumab is a humanized monoclonal antibody. It is recommend for patients with relapse after the first line of therapy to MS and for patients with an aggressive MS at the diagnosis. The aim of this study was to describe the profile of patients in use of natalizumab from 12/2013 until 15/2015 in follow-up at Hospital de Base – Distrito Federal.

Material e Método / Material and method: Retrospective analysis of 36 patients diagnosed with relapsing-remitting form (RRMS) or secondary progressive (SPMS) who were treated with natalizumab. Analyzing annualized relapse rate (ARR), disability (Expanded Disability Status Scale score) and other variables.

Resultados / Results: There were 36 patients, 28 (77.7%) women and 8 (22,3%) men with an average age of 39.5 years. 83.3% of the patients had the EMSR form and 16,7% SPMS form. The average interval between diagnosis and the start of the use of natalizumab was 6.5 years, with a range of 1 - 22 years. The annual relapse rate (TRA) was analyzed 2 years previous treatment with natalizumab, showed the total of 35 relapses, with TRA-annual of 0,9. During the use of the drug there was only one clinical relapse in our sample. From 20 patients who made a MRI after 12 months of treatment, 17 (85%) showed no radiographic progression, 2 (10%) showed contrast enhanced injuries and 1 showed one new lesion on T2 - Flair. The mean EDSS at onset of treatment was 5.5, including all the subjects. Considering the group of patients who completed treatment, the initialmedium EDSS was 6.2 and the final medium EDSS was 5.6. Moreover, those who used the natalizumab for at least 12 months, started with EDSS 5.85 and were with EDSS 5.5 after a media of 21.1 infusions.

Discussão e Conclusões / Discussion and Conclusions: The profile of our patients is similar to the current in literature. In our experience, treatment with Natalizumab was effective in control the disease progression, though the small number of patients limited the statistical significance of our results.

Palavras Chave / Key-Words: Multiple Sclerosis, Natalizumab

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Sala / Room: Auditorium

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Autores / Authors: da Fonseca, B A , Pereira, C B , Jorge, F M H , Simm, R , Apóstolos-Pereira, S , Callegaro, D

Instituições / Institutions: University of São Paulo Medical School - Sao Paulo - Brasil

Título / Title: Inability to reweight sensory information reduces postural balance in multiple sclerosis patients

Introdução / Introduction: Balance and mobility limitations are a hallmark of patients with multiple sclerosis (PWMS), independent of disability level. Adequate balance relies on accurate perception of sensory information by somatosensory, vestibular and visual systems. The process of adjusting the sensory contributions to postural balance is referred to as sensory reweighting; this means that when one sensory cue is absent or inappropriate, the CNS uses other more reliable cues. Thus, our aim was to investigate if PWMS can correctly reweight sensory information during different sensory conditions to maintain balance control.

Material e Método / Material and method: We evaluated 70 PWMS (EDSS 0 – 4.0). They were divided into two groups according to their self-report about postural balance: without balance problem (w/oBP, n=38) and with balance problem (wBP,n=32). We excluded patients with dizziness, cognitive and visual impairment. Balance was tested with the Sensory Organization Test (SOT) of Computerized Dynamic Posturography, which was developed to identify the relative contribution of the 3 main sensory systems involved in balance. Statistical analysis was performed by the Kruskal Wallis test and logistic regression.

Resultados / Results: wBP group showed poorer balance performance across all conditions tests with significant group differences ($p<0,01$). Logistic regression showed that SOT outcomes have had 79% of sensibility to detect correctly patients with balance problem.

Discussão e Conclusões / Discussion and Conclusions: In the absence of visual/vestibular impairment, the inability to maintain balance on unstable surface is related to inadequate reweight. Inefficient central processing and integration of sensory input may contribute to poor balance in MS, probably due to MS-related lesions in the cerebellum and brain stem, leading to difficulties in the integration of vestibular inputs. SOT allows us to detect patients with imbalance and those unable to reweight sensory inputs when environment changes.

Palavras Chave / Key-Words: Multiple Sclerosis, postural balance, posturography, sensory integration, risk of falls.

Código / ID: PO 017

Data / Date: 2015-08-21

Horário / Time: 16:30:00 às 18:00:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: POSTER

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Instituições / Institutions: HUAP-Universidade Federal Fluminense-UFF - Rio de Janeiro - Brasil

Título / Title: Gait in MS patients: A deeper look

Introdução / Introduction: Multiple sclerosis's (MS) symptomatology strongly interferes with one's functional capacity. Several factors regarding gait can be affected, such as speed, stride length, maximum distance and balance.

Material e Método / Material and method: 40 MS patients (patient group) and 40 healthy subjects (control group) were evaluated using Time Up and Go (TUG), Tinetti and 25-Foot Walk (T25FW) tests and EDSS scale. None of the participants reported fatigue between tests. This study will focus on the following comparisons: test results with EDSS, results of all three tests, test results of the patient and control groups, test results with the patient group's age and test results with illness duration.

Resultados / Results: Based on statistical data, there are moderate to high correlations between EDSS (Mean=3.03) and TUG (Mean=11.92), T25FW (Mean=7.56) and Tinetti (Mean=24.41) tests. The patient group reported longer execution times for TUG and T25FW tests and lower scores on the Tinetti test than the control group. A direct correlation was found between illness duration (Mean=11.09), EDSS, TUG execution time, T25FW execution time and Tinetti score. Regarding risk of fall, the patient group was divided into three types of risk: mild (50%) (Mean=38.00), moderate (30%) (Mean=43.67) and severe (20%) (Mean=47.25). Age (Mean=41.55) did not correlate with these risks, as the average age for each is similar.

Discussão e Conclusões / Discussion and Conclusions: The EDSS scale depends greatly on the evaluator's interpretation and not on tangible data. Thus, it is necessary to utilize more accurate tests to evaluate characteristics of gait. This study demonstrates that all tests need to be evaluated together, as each approaches different aspects. It also shows that age does not contribute to risk of falls, even though aging is a factor known for this increased risk. Functional assessment is essential in clinical practice. Proper gait and fall risk evaluations are important factors in order to avoid complications that are not related to MS.

Palavras Chave / Key-Words: Gait, MS, TUG, EDSS, Tinetti

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Budib, M B , Felisbino, I , Zulin, M i , Hashiguchi, M M

Instituições / Institutions: Hospital São Julião - Mato Grosso do Sul - Brasil

Título / Title: Functional capacity and quality of life of patients with Multiple Sclerosis: A Literature Review

Introdução / Introduction: Multiple Sclerosis (MS) is a demyelinating disease of the central nervous system that affects primarily young women. The most common symptoms are: visual disturbances, paresthesia, paresis and fatigue. This study aims to draw a physical therapy profile that provides improved functional capacity and quality of life of people with MS.

Material e Método / Material and method: Literature review with randomized and non-randomized controlled trials published in scientific journals between 2010 and 2015, abording subjects with MS who used exercise alone or combined with other therapies. The search was carried out by means of electronic databases Scielo, PEDro, Bireme and PubMed, according to descriptions of Medical Subject Heading Terms (MeSH): Exercise and Multiple Sclerosis, Multiple Sclerosis and Physiotherapy, Physical Activity and Multiple Sclerosis and Therapeutic Exercise and Multiple Sclerosis.

Resultados / Results: The articles showed that resistance exercises for lower limbs improved gait, strength, fatigue and functionality. Resistance training and stretching have shown good results for functionality and mobility. To reduce pain, the articles showed that the best results are obtained with hydrotherapy, which also led to increased quality of life. The use of the vibrating platform improves strength, fatigue and balance only if associated with isotonic exercises. As for the intensity of the exercises, mild, moderate and alternating intensity are well tolerated by subjects with MS, and high-intensity exercise led to increased pain and increased withdrawal of therapy. The survey also showed that exercises supervised by physiotherapists have better results than just driven home exercises.

Discussão e Conclusões / Discussion and Conclusions: Muscular strengthening exercises, stretching and gait training, supervised by physical therapists, are beneficial to improving the quality of life, pain, functionality, mobility, balance, fatigue, fear of falling and strength in subjects with MS.

Palavras Chave / Key-Words: Exercise, Multiple Sclerosis, Physiotherapy, Physical Activity and Therapeutic Exercise.

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Castro, A H A , Campos, W R , Santos, D V , Lana-Peixoto, M A

Instituições / Institutions: CIEM MS Research Center, Federal University of Minas Gerais Medical School - Minas Gerais - Brasil, Division of Uveitis, Federal University of Minas Gerais Medical School - Minas Gerais - Brasil

Título / Title: PREVALENCE OF THE ASSOCIATION OF MULTIPLE SCLEROSIS AND INTERMEDIATE UVEITIS IN BRAZIL IS LOW AS COMPARED WITH INTERNATIONAL SERIES

Introdução / Introduction: Intermediate uveitis (IU) is a chronic intraocular inflammatory disorder in which the vitreous represents the major site of inflammation. It may be associated with a variety of systemic diseases including sarcoidosis, Lyme disease, syphilis and multiple sclerosis (MS) Numerous international studies have looked into the association between MS and IU but, to our knowledge, the prevalence of this association has not yet been systematically investigated in Brazil.

Material e Método / Material and method: OBJECTIVE: To compare the prevalence of the association of MS and IU in patients consecutively examined at a MS referral center and at a uveitis referral center in Brazil with those reported in other countries. METHODS: We reviewed the medical records of 1429 patients with suspected demyelinating diseases of the CNS at CIEM MS Research Center and of 218 patients with the diagnosis of IU seen at the Uveitis Division of Hospital São Geraldo (HSG) of the Federal University of Minas Gerais, in Belo Horizonte, Brazil. Patients were included in the study if they met both McDonald 2010 criteria for diagnosis of MS and the Standardization of Uveitis Nomenclature (SUN) 2005 criteria for diagnosis of IU (including pars planitis -PP). Medline, Ibecs and Lilacs were searched using the key words: “multiple sclerosis”, “relapsing-remitting multiple sclerosis, “primary progressive multiple sclerosis” “demyelinating disease”, “uveitis”, “intermediate uveitis” and “pars planitis”. We also used the references of papers and textbooks.

Resultados / Results: Only one patient examined at both Centers had the association of MS and IU with a prevalence of 0.4% of IU and 0,6% of the PP cases. Four papers reported the frequency of the association of MS and PP (12% and 12.5% in the USA; 4.2% in Spain; 15.9% and 30.4% in another Spanish study by retrospective and prospective analysis). Five papers reported the frequency of association of MS and IU as 7.2% and 16.7% in USA; 6.9% in Slovenia; 10.5% in Germany and 4.2% in Iran. In four papers the uveitis classification was not informed and the prevalence rates found were 1.3% and 1% in USA; 1.4% in a German-American collaborative study and 1% in Austria.

Discussão e Conclusões / Discussion and Conclusions: The prevalence of the association of MS and IU or PP is very low in Brazil as compared with series from other countries. Reasons for this difference warrant further investigation.

Palavras Chave / Key-Words: Key-Words: Multiple sclerosis; intermediate uveitis; pars planitis.

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Chalub, S , Talim, N C , Freitas, H , Amaral, J M S S , Talim, L E C , Kleinpaul, R , Lana-Peixoto, M A

Instituições / Institutions: CIEM MS Research Center - Minas Gerais - Brasil

Título / Title: THE MS SUBOPTIMAL TREATMENT OUTPATIENT CLINIC : RATIONALE, METHODOLOGY AND STRATEGY OF ESCALATION THERAPY

Introdução / Introduction: The most effective treatment of disease activity in multiple sclerosis (MS) may be a key factor in prevention of an unfavorable outcome, particularly in the early phases of the disease. Early identification of failure of disease-modifying therapies (DMT) may prompt appropriate medical intervention providing patients with the best available care. As MS treatment is rapidly evolving and new drugs are added to therapeutic armamentarium, clinicians face, on the other hand, a more complex scenario to take decisions and make choices. A specific MS Outpatient Clinic with focus on treatment failure – the MS Suboptimal Treatment Outpatient Clinic – was then set at CIEM MS Research Center of the Federal University of Minas Gerais Medical School to see patients in whom disease activity has been identified in spite of use of DMT. OBJECTIVE: To describe the rationale, methodology of patients selection and evaluation, as well as strategy of escalation therapy for suboptimal responders to first-line DMT at CIEM MS Suboptimal Treatment Outpatient Clinic.

Material e Método / Material and method: All MS patients seen at CIEM MS Research Center with suspected suboptimal response to DMT in association with evidence of clinical or MRI disease activity were referred to the MS Suboptimal Treatment Outpatient Clinic. The Canadian Multiple Sclerosis Working Group (2004) framework is used considering relapse rate, severity, and extent of recovery as important factors when judging treatment response. The Río et al. 2009 criteria for suboptimal treatment has been used.

Resultados / Results: The MS Suboptimal Treatment Outpatient Clinic at CIEM MS Research Center has been working for over one year.

Discussão e Conclusões / Discussion and Conclusions: Special attention to assess treatment response to DMT has enabled doctors at CIEM MS Research Center to identify non-reponders at an early stage of treatment and switch medication according to severity of disease activity and disability progression.

Palavras Chave / Key-Words: multiple sclerosis, suboptimal treatment, disease-modifying-therapy

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Going, L C , Lourido, A M , Berlim, L V , Egas, M B A , Souza, M R , Fragoso, Y D

Instituições / Institutions: Universidade Católica de Santos - Sao Paulo - Brasil, Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Aggressive behavior is uncommon in patients with multiple sclerosis

Introdução / Introduction: Patients with multiple sclerosis (MS) have been reported to be more aggressive than the general population. Aggressive behavior is not necessarily related to bad attitudes; in fact, aggression is frequently assertive and necessary for establishing our space in society. However, aggression may have a complete different connotation and become an unacceptable behavior if directed against others, hurting and offending them.

Material e Método / Material and method: Twenty-four patients with MS and 24 age and gender matched healthy controls were assessed using the “Scale for Assessment of Aggressive Tendency (EATA)”. Individuals with moderate to severe depression and /or anxiety were excluded from assessment with EATA.

Resultados / Results: Patients with MS showed significantly less aggressive behavior than did the control group. Half the patients with MS had lower than average aggressive behavior, and many of them reported a change in attitudes after the diagnosis of MS. These patients reported that they knew that emotional stress could trigger clinical relapses of MS and avoided situations that might generate such stress. Another common report from the patients with MS was that someone in the family took the role of “aggression, confrontation, defense of interests” on behalf of the patient. There was no correlation between aggressiveness, MS disease duration or MS-related disability.

Discussão e Conclusões / Discussion and Conclusions: Previous reports of an increased aggressive behavior in patients with MS were not confirmed in the present study. A reduced aggressive behavior in MS seems to be a more reasonable result for a patient who is typically young and suffers from a chronic and potentially disabling condition. Giving up on assertiveness and fights in life are expected in case of severe diseases.

Palavras Chave / Key-Words: multiple sclerosis; aggression; depression; behavior

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Ribeiro, R A , Costa, C , Franco, C R , Fragoso, Y D

Instituições / Institutions: Universidade de Sao Paulo - Sao Paulo - Brasil, Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Dental care in patients with multiple sclerosis: newer medications demand more attention

Introdução / Introduction: The treatment of multiple sclerosis (MS) has reached an era of newer and more potent medications that typically alter the number and/or functions of lymphocytes. Although patients are screened for a variety of potential infectious diseases that may reactivate in the presence of lymphocyte dysfunction, dental care is not always taken into consideration. Patients may have a variety of oral infections that might affect (and be affected by) the medications that alter lymphocytes. The objective of the present study was to report on the dental conditions of patients with MS undergoing newer treatments, i.e., fingolimod and natalizumab.

Material e Método / Material and method: Patients attending the MS Reference Center in Santos, SP, who were in use of fingolimod or natalizumab, were invited for a complete oral and dental evaluation, including panoramic radiographies.

Resultados / Results: At present, 10 patients have been assessed (5 on fingolimod, 5 on natalizumab), 3 males and 7 females, using the drug for an average of 11 months. They all had regular consultations with the dentist, and tried to have at least one routine consultation per year. Three patients had caries (one of them had 6 caries), and none had dental infections. Periodontal index showed that only 2 patients were in very good condition, while 4 had significant gum retraction. All patients were offered dental treatment and follow-up.

Discussão e Conclusões / Discussion and Conclusions: Dental care in MS is very important, as the oral cavity may be a source of infection that might negatively affect the outcome of MS treatment.

Palavras Chave / Key-Words: multiple sclerosis; dentist; caries, periodontal disease

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Fragoso, Y D , Alves-Leon, S V , Barreira, A A , Callegaro, D , Ferreira, M L B , Finkelsztejn, A , Gomes, S , Gonçalves, M V M , Machado, M I M , Marques, V D , Matta, A P d C , Papais-Alvarenga, R M , Pereira, S L A , Tauil, C B , Sato, H

Instituições / Institutions: , Hospital das Clinicas, Universidade de Sao Paulo - Sao Paulo - Brasil, Hospital Beneficencia Portuguesa São Paulo - Sao Paulo - Brasil, Hospital de Base do Distrito Federal - Distrito Federal - Brasil, Hospital de Clinicas de Porto Alegre - Rio Grande do Sul - Brasil, Hospital Paulistano - Sao Paulo - Brasil, Hospital Regional Hans Dieter Schimid - Santa Catarina - Brasil, Ibstitute of Neurology, Curitiba - Parana - Brasil, Universidade de Sao Paulo, Ribeirao Preto, - Sao Paulo - Brasil, Universidade Federal do Estado do Rio de Janeiro - Rio de Janeiro - Brasil, Universidade Federal do Rio de Janeiro - Rio de Janeiro - Brasil, Universidade Federal Fluminense - Rio de Janeiro - Brasil, Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Fingolimod prescribed for the treatment of multiple sclerosis in patients before the age of 18 years.

Introdução / Introduction: There have been no clinical trials for approval of medications for treating multiple sclerosis in patients under the age of 18 years. All treatments are based on personal experience and data from open observational studies. Fingolimod is an oral drug for treating multiple sclerosis that has proven to be efficient and safe in adults. The aim of the present study was to report on patients with multiple sclerosis who started treatment with fingolimod before the age of 18 years.

Material e Método / Material and method: Eighteen patients treated with fingolimod were identified in the Brazilian database of children and adolescents with multiple sclerosis. The average time of use of the drug was 8.5 months.

Resultados / Results: Fingolimod showed a good safety and efficacy profile in these patients, all of whom had very active multiple sclerosis. After starting treatment with fingolimod, only one patient had a relapse and a new lesion on MRI. The patients' degree of disability did not progress. No major adverse events were reported in relation to the first dose of the drug, nor in the short and medium-term treatment. No patient has been followed for longer than 18 months, thus limiting long-term conclusions.

Discussão e Conclusões / Discussion and Conclusions: Off-label use of fingolimod in patients before the age of 18 years was shown to be a good therapeutic option for multiple sclerosis control.

Palavras Chave / Key-Words: multiple sclerosis; children; adolescentes; fingolimod

Código / ID: PO 025

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Diegues, M C D C A , Pascoal, E G T , Ruiz, C A C , Fragoso, Y D

Instituições / Institutions: Hospital de Olhos Grottone - Sao Paulo - Brasil, Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Ophthalmological findings in a longitudinal study of patients with multiple sclerosis

Introdução / Introduction: Patients with multiple sclerosis (MS) often present abnormalities in the ophthalmological examination. Apart from optical neuritis, these patients have changes in the retinal fiber layers and compromised quality of vision.

Material e Método / Material and method: Patients undergoing treatment in the MS Reference Center in Santos were offered regular consultations with a group of ophthalmologists who are particularly interested in MS. After one year of the initial evaluation, the patients were offered a new consultation and testing with the same ophthalmologists. Tests included biomicroscopy, assessment of visual acuity, fundoscopy, and the Ishihra test. Specific questionnaires regarding visual complaints were also included.

Resultados / Results: At present, 13 patients have completed two examinations with a year interval between them. None of them had a new relapse (and no optical neuritis) in the year interval. After one year, a large number of patients with MS had specific and inespecific visual complaints (71%), with 14.3% presenting worse visual acuity, 28.6% showing alterations in fundoscopy and 28.6% presenting worse performance in the Ishihara testing. One quarter of this group has visual limitations that can affect their independence. Even with this kind of result, only a third of patients maintain regular consultations with ophthalmologists.

Discussão e Conclusões / Discussion and Conclusions: Patients MS must have regular follow-up consultations in the ophthalmology department. Although many doctors and patients may consider optical neuritis to be the only reason for a consultation with a specialist, it is important for all patients to be regularly seen by ophthalmologists with study MS.

Palavras Chave / Key-Words: multiple sclerosis; eye; ophthalmology; visual

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Gonçalves, M L L , França, C M , Almeida, L , Bussadori, S K , Fragoso, Y D

Instituições / Institutions: Universidade Metropolitana de Santos - Sao Paulo - Brasil, Universidade Nove de Julho - Sao Paulo - Brasil

Título / Title: Orofacial Evaluation in Patients with Multiple Sclerosis Using the Nordic Orofacial Test-Screening

Introdução / Introduction: Patients with multiple sclerosis (MS) have been reported to have worse oral health than the general population. The objective of this study was to investigate whether patients with MS have more orofacial dysfunctions through the Nordic Orofacial Test-Screening (NOT-S).

Material e Método / Material and method: Transversal study, assessed by questionnaires. Disability and disease duration were assessed for patients, in order to establish whether these parameters would affect results of NOT-S.

Resultados / Results: NOT-S results were compared between 34 patients with MS and 34 control subjects matched for age, gender and socioeconomic level. There was no significant difference in the orofacial function of patients with MS and control subjects. Results did not show statistically significant correlation between disability and NOT-S or disease duration and NOT-S. However, the correlation between the disease's duration and the degree of disability was statistically significant (p=0.0004), thus suggesting that the results are in accordance to what was expected regarding MS. In this particular population, every year of MS disease was associated to a worsening of 0.33 points in EDSS.

Discussão e Conclusões / Discussion and Conclusions: These results indicate no correlation between orofacial dysfunctions and MS. The fact that patients with MS were undergoing treatment, regular consultations and assessments with a multidisciplinary team may have positively affected the results.

Palavras Chave / Key-Words: multiple sclerosis; dental care; oral fuctions

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Data / Date: 2015-08-21

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Sala / Room: Auditorium

Forma de Apresentação / Presentation: POSTER

Autores / Authors: Spessotto, C V , Fragoso, Y D

Instituições / Institutions: Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Patient Satisfaction with Multiple Sclerosis Treatment

Introdução / Introduction: Treatments for Multiple Sclerosis (MS) are expanding and new forms of use have been proposed. This may influence adherence by the patient to the treatment proposed by the doctor, which might be conventional (by injection: intramuscular or subcutaneous), infusion or oral. The aim of this study was to evaluate treatment satisfaction with the various forms of MS treatment available today.

Material e Método / Material and method: In this cross-sectional study, 28 patients undergoing MS treatment with at least three consecutive months of therapy were prospectively evaluated, and each of them answered a questionnaire of 25 items, measured on a standardized Likert scale. This project was approved by the research ethics committee of UNIMES. This was a pilot project, and the first results are presented here.

Resultados / Results: The patients had been undergoing treatment for between 3 months and 15 years, with different drugs to control MS. Two thirds of the patients considered that the efficacy and safety of the medications used was good or excellent, without any embarrassment or negative effect caused by the injectable medications. The level of adherence to the treatment was high among these patients: 100% of them regularly made use of at least 80% of the medication dose (access criteria defined by the World Health Organization).

Discussão e Conclusões / Discussion and Conclusions: Patients with multiple sclerosis treated at the Reference Center for Neuroimmunology in Santos are satisfied with their treatment and present good adherence. This project will continue to include more patients in the region and will be extended to other units in Brazil.

Palavras Chave / Key-Words: multiple sclerosis; interferon; glatiramer acetate; fingolimod; natalizumab

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Data / Date: 2015-08-21

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Sala / Room: Auditorium

Forma de Apresentação / Presentation: POSTER

Autores / Authors: Olmo, N R S , Melo, S T L , Brito, L A , Fragoso, Y D

Instituições / Institutions: Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Patients with multiple sclerosis present more chronic and recurrent pain than a control population

Introdução / Introduction: Patients with multiple sclerosis (MS) are reported to be more affected by pain than the general population. Although neuropathic pain may be the first idea that comes to mind as a manifestation of MS, other types of pain can be present and significantly compromise quality of life.

Material e Método / Material and method: Cross-sectional case-control study, assessing the presence and characteristics of pain in patients with MS and matched control subjects. Interviews were conducted individually with MS patients and matched controls (1:2). The presence of painful conditions lasting for at least three months (continuously or recurrently) was assessed. Participants were assessed for mood disorders (depression, anxiety) and pain, using validated instruments. Only patients who had not experienced a clinical relapse over the previous three months were included.

Resultados / Results: Thirty-three patients with MS and 66 controls were enrolled in the study. Ninety percent of the patients with MS reported having one or more types of chronic pain. Among the controls, the prevalence of chronic pain was 10.6%. Headache (48%), joint pain (21%) and backache (15%) were the most frequent complaints among the patients, and the intensity of pain was moderate or severe in 78.8% of all individuals with MS. Anxiety, depression and the use of tobacco, illicit drugs, depression or anxiety were similar between the groups of patients and controls.

Discussão e Conclusões / Discussion and Conclusions: The results from the present study indicate that the most painful conditions among patients with MS were not of neuropathic or demyelinating origin and, therefore, they were similar to what is found in the general population, albeit with greater prevalence.

Palavras Chave / Key-Words: multiple sclerosis; pain; alcohol; illicit drugs.

Código / ID: PO 029

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Sala / Room: Auditorium

Forma de Apresentação / Presentation: POSTER

Autores / Authors: Cardoso, M , Olmo, N R S , Fragoso, Y D

Instituições / Institutions: Instituto de Pesquisa e Ensino Médico do Estado de Minas Gerais - Minas Gerais - Brasil, Multimagem Santos - Sao Paulo - Brasil, Neuroimmunology Angiocorpore - Sao Paulo - Brasil, Universidade Metropolitana de Santos - Sao Paulo - Brasil

Título / Title: Systematic review of cognitive dysfunction in pediatric and juvenile multiple sclerosis

Introdução / Introduction: Cognitive dysfunction is a common finding in multiple sclerosis (MS). While very disruptive in adults with MS, cognitive impairment may drastically affect the life of younger patients with MS who are still undergoing education and schooling.

Material e Método / Material and method: A systematic review following the PRISMA recommendations was carried out assessing published data on MS and cognition in pediatric or juvenile patients. Using the PICO framework, the authors independently searched for the terms “cognition” OR “memory” AND “children” OR “pediatric” OR “juvenile” OR “adolescents” AND “multiple sclerosis” OR “MS” in the following databases: Medline, Pubmed, Scopus, Index Medicus, Biomed Central, LILACS, Scielo, Google Scholar, and the Cochrane Database of Systematic Reviews.Only papers presenting original data on patients with MS diagnosed before the age of 18 years were included.

Resultados / Results: The active search found 183 studies between this paper in published in September 1999 and March, 1st, 2015. Thirty-two papers fulfilled the inclusion criteria for this systematic review. The conclusion from all papers was that cognitive dysfunction in MS starting before the age of 18 years is significant and disruptive, and must be routinely assessed. However, methods for assessment were heterogeneous, often extensive and very expensive to perform, while proposals for treatment were virtually absent in the literature.

Discussão e Conclusões / Discussion and Conclusions: Several papers on the subject of cognitive dysfunction in pediatric and juvenile MS have been published over the last decades. Complex attention, information processing speed, executive functions, linguistic abilities, verbal and visual memory, reasoning, and problem solving are all potentially affected by MS in this population. Cognitive dysfunction in pediatric and juvenile MS needs to be studied in a task-force manner, with a collaborative group from specialized MS Units.

Palavras Chave / Key-Words: multiple sclerosis; cognition; memory; children; adolescents.

NMO, ADEM and CIS

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Horário / Time: 14:45:00 às 15:00:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: PLATFORM

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Título / Title: Astrocyte and Myelin Injury in Neuroinflammatory Disorders with Myelin Oligodendrocyte Glycoprotein or Aquaporin-4 Antibody Positive Cerebrospinal Fluid

Introdução / Introduction: To evaluate astrocyte and myelin injury in inflammatory central nervous system disorders with positivity to antibodies against aquaporin-4 (AQP4) or myelin-oligodendrocyte glycoprotein (MOG) in the cerebrospinal fluid (CSF).

Material e Método / Material and method: We enrolled 59 anti-AQP4+ and 30 anti-MOG+ seropositive patients with stored CSF samples from Japan, Brazil, France, South Korea, Austria, Spain and Thailand. CSF was blindly tested for anti-AQP4 and anti-MOG using cell-based assays. Astrocyte and myelin damage was evaluated measuring glial fibrillary acidic protein (GFAP) and myelin basic protein (MBP) respectively using commercial ELISA.

Resultados / Results: Among 89 patients with serum positivity to anti-AQP4 or anti-MOG, 67 were positive in the CSF, representing 76% of anti-AQP4+ (45/59) and 76% of anti-MOG+ (22/30) cases. All antibody results in their CSF identified the same antibody present in sera. No CSF samples were positive for both antibodies. The median GFAP level in the CSF was remarkably elevated in the anti-AQP4+ CSF compared to anti-MOG+ CSF ($p < 0.0001$). On the other hand, elevation of MBP was similar between AQP4+ and MOG+ patients ($p=0.6531$). The concentration of GFAP correlated with anti-AQP4 titers in the CSF (Spearman rho = 0.5, $p = 0.0005$), especially in samples collected after few days from attack and before any treatment.

Discussão e Conclusões / Discussion and Conclusions: Astrocyte damage is evident in anti-AQP4+ CSF, and anti-AQP4 titers in the CSF correlates with GFAP levels. The level of myelin damage is similar between these two groups. The absence of elevated GFAP suggests a distinct underlying mechanism in anti-MOG+ cases causing myelin damage.

Palavras Chave / Key-Words: antibody, aquaporin-4, myelin-oligodendrocyte glycoprotein, neuromyelitis optica, multiple sclerosis, acute disseminated encephalomyelitis

Código / ID: PL 004

Data / Date: 2015-08-20

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Sala / Room: Auditorium

Forma de Apresentação / Presentation: PLATFORM

Autores / Authors: Talim, N C , Talim, L E C , Kleinpaul, R , Amaral, J M S S , Prates, M , Lana-Peixoto, M A

Instituições / Institutions: CIEM MS Research Center, Federal University of Minas Gerais Medical School - Minas Gerais - Brasil

Título / Title: CLINICAL CHARACTERIZATION OF THE AREA POSTREMA SYNDROME IN NEUROMYELITYS SPECTRUM DISORDERS PATIENTS

Introdução / Introduction: Recently area postrema, the emetic reflex center in the central nervous system, located at the floor of the fourth ventricle, has been recognized as one of the preferential targets for AQP4-IgG attacks in neuromyelitis optica spectrum disorders (NMOSD). Although a number of papers have emphasized the relevance of intractable hiccups, nauseas/vomiting - the area postrema syndrome (APS) - as one of the most typical components of the spectrum of the disease demographic and clinical characterization of NMOSD with APS are still scanty in the literature.

Material e Método / Material and method: Objective: To describe the frequency and characteristics of APS in NMOSD with brainstem involvement. Patients and Methods: Selected patients from CIEM MS Research Center met the 2006 revised criteria for diagnosis of NMO or Wingerchuk 2007 definition of NMOSD and presented symptoms related to brain stem involvement either as the inaugural manifestation of the disease or during its course. Area postrema syndrome was defined as the occurrence of intractable hiccups, nausea and vomiting for periods equal to or longer than three days. Cell-based assay was used for serum detection of anti-AQP4 antibody.

Resultados / Results: Results: Out of 109 NMOSD patients who presented signs of brain stem involvement 58 (53.2%) had a positive history of intractable hiccups, nausea/vomiting episodes. Patients' median age at disease onset was 27.5 (10–56) years and there were 53 (91.4%) females, 41 Blacks/ Mulattoes, and 17 Caucasians. Aquaporin 4-antibody seropositive status was found in 45 patients, 32 (71.1%) of them were non-Caucasians. In 18 patients area postrema involvement was characterized by hiccups and nauseas/vomiting; 37 had nauseas/vomiting but no hiccups, whereas three patients had intractable hiccups without nauseas/vomiting. Such episodes lasted from few days to weeks. In 36 patients APS occurred as the inaugural manifestation of NMOSD (in 18 it was an isolated symptom, whereas in the remaining 18 patients it was associated with optic neuritis and/or transverse myelitis).

Discussão e Conclusões / Discussion and Conclusions: Conclusion: Area postrema syndrome is a rather typical phenomenon occurring most frequently in females, non-Caucasians and anti-AQP4 antibody seropositive NMOSD.

Palavras Chave / Key-Words: Key-Words: Neuromyelitis optica spectrum disorders; area postrema syndrome; intractable nausea/vomiting and hiccups; anti-aquaporin 4-antibody; optic neuritis; transverse myelitis Acknowledgments: We thank Prof. K. Fujihara and Dr. D. Sato for help with the AQP4-IgG cell-based assays.

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Data / Date: 2015-08-20

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Sala / Room: Auditorium

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Autores / Authors: Talim, N C C , Talim, L E C , Kleinpaul, R , Amaral, J M S S , Lana-Peixoto, M A

Instituições / Institutions: CIEM MS Research Center, Federal University of Minas Gerais Medical School - Minas Gerais - Brasil

Título / Title: DISTURBANCES OF OCULAR MOTILITY IN NEUROMYELITIS OPTICA SPECTRUM DISORDERS

Introdução / Introduction: Although optic neuritis is one of the most frequent clinical elements of neuromyelitis optica spectrum disorders (NMOSD) a number of eye movement disturbances may cause visual discomfort and disability. Ocular movement disorders in NMOSD usually result from lesions located in pons and midbrain and occur in association with other signs of brainstem involvement.

Material e Método / Material and method: We reviewed the medical records of patients examined at CIEM MS Research Center who met Wingerchuk's 2006 diagnostic criteria for definite NMO and 2007 definition of NMOSD. Patients with any evidence of eye movement disorder were analyzed regarding demography, clinical characterization of ocular motility and aquaporin-4 antibody (AQP4-IgG) serum status. Cell-based assay and indirect immunofluorescein assay were used to test AQP4-IgG serum status.

Resultados / Results: Out of 255 patients with NMOSD 109 presented brainstem symptoms and 25 (22.9%) had a disorder of ocular motility. Patients with eye movement disorders were 19 females; 11 Whites, 12 Mulattos and two Blacks). The median age at disease onset was 25 (3-52) years. Diplopia occurred in 24 patients and one patient complained of oscillopsia. Horizontal nystagmus was found in 1 patient, ptosis in 3, sixth nerve palsy in 5, and horizontal conjugate gaze palsy in 2. In 15 patients who had transient diplopia during a NMOSD attack objective examination disclosed no eye movement abnormalities. Seropositive AQP4-IgG status was observed in 15 (60%) patients.

Discussão e Conclusões / Discussion and Conclusions: Disturbances of ocular motility are not rare phenomena in NMOSD patients and may occur in a variety of clinical presentations. Although in most patients they are transient, they may persist increasing patients' disability.

Palavras Chave / Key-Words: Key-Words: Neuromyelitis optica spectrum disorders; anti-aquaporin 4-antibody; disturbances of ocular motility; brainstem symtoms. Acknowledgments: We thank Prof. K. Fujihara and Dr.D. Sato for help with the AQP4-IgG cell-based assays.

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Data / Date: 2015-08-20

Horário / Time: 15:45:00 às 16:00:00

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Forma de Apresentação / Presentation: PLATFORM

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Instituições / Institutions: CIEM MS Research Center, Federal University of Minas Gerais Medical School - Minas Gerais - Brasil, University of São Paulo Medical School - Sao Paulo - Brasil

Título / Title: NEUROMYELITIS OPTICA SPECTRUM DISORDERS PHENOTYPE IN ANTI-MOG SEROPOSITIVE PATIENTS

Introdução / Introduction: Neuromyelitis optica spectrum disorders (NMOSD) are frequently associated with anti-aquaporin 4 (anti-AQP4) autoimmunity. Recently, some patients with full or limited NMOSD phenotype who are seropositive to myelin oligodendrocyte glycoprotein antibody (anti-MOG IgG) and seronegative to anti-AQP4 IgG have been described in different countries suggesting that this association is a worldwide phenomenon, occurring in most ethnic groups. Herein we describe a series of patients who exhibited NMOSD phenotype and were found to be anti-AQP4 IgG seronegative and anti-MOG IgG seropositive. The present series is compared to cases previously reported in the literature.

Material e Método / Material and method: Patients were examined at CIEM MS Research Center in Belo Horizonte, and Hospital das Clinicas of the University of Sao Paulo, in Sao Paulo, Brazil. Selected patients presented at least one of the cardinal manifestations of NMO (recurrent or bilateral simultaneous optic neuritis (ON) or longitudinally extensive transverse myelitis (LETM)). Patients' sera were tested for anti-AQP4 IgG and anti-MOG IgG by cell-based assay. We searched the PubMed for papers on anti-MOG IgG associated with NMOSD phenotype. References from relevant articles were also used.

Resultados / Results: Our series comprise 31 anti-MOG seropositive patients with NMOSD phenotype (19 were females, 18 had ON, 8 LETM, and 5 had both ON and LETM). Median age at disease onset was 32 (3-52) years. Transverse myelitis involved the cervical cord in 4, thoracic in 9 and lumbar in 3. Brain MRI was normal in 13/30 patients. Cerebrospinal fluid oligoclonal bands (CSF OCB) were absent in 5/5 patients. The literature search yielded 9 published papers which described 51 patients (26 females, median age 31 years, 17 exclusively with ON, 16 with TM, and 15 with ON+TM). Cervical cord was involved in 75% of cases whose spinal MRI was described, thoracic in 87% and lumbar in 45%. Brain MRI was normal in in 56%. CSF BOC was absent in 35/42 patients.

Discussão e Conclusões / Discussion and Conclusions: Compared with previously reported international series, Brazilian patients with anti-MOG IgG and NMOSD phenotype more frequently are females, and have restricted phenotype (most frequently isolated ON). On the other hand, they had less commonly lesions in the cervical and lumbar cord.

Palavras Chave / Key-Words: KEY-WORDS: Neuromyelitis optica spectrum disorders; anti-aquaporin 4-antibody; myelin oligodendrocyte glycoprotein antibody; optic neuritis; longitudinally extensive transverse myelitis Acknowledgments We thank Prof. K. Fujihara and Dr. D. Sato for help with the AQP4-IgG cell-based assays.

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Data / Date: 2015-08-20

Horário / Time: 16:00:00 às 16:15:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: PLATFORM

Autores / Authors: Freitas, H , Kleinpaul, R , Talim, N C , Amaral, J M S S , Talim, L E C , Chalub, S , Prates, M , Lana-Peixoto, M A

Instituições / Institutions: CIEM MS Research Center - Minas Gerais - Brasil

Título / Title: AREA POSTREMA SYNDROME AS PREDICTIVE FACTOR OF OUTCOME IN NEUROMYELITIS OPTICA SPECTRUM DISORDERS

Introdução / Introduction: Neuromyelitis optica spectrum disorders (NMOSD) are mostly frequent characterized by attacks of optic neuritis and transverse myelitis that may cause severe disability. Identification of predictive factors of outcome may provide physicians with tools to develop strategies to choose prophylactic treatments more timely and appropriately. Area postrema syndrome (APS) has recently been recognized as a frequent sign of dorsal brainstem involvement in NMOSD patients. It more commonly occurs in AQP4-IgG seropositive patients and may be the inaugural symptom of the disease or even antedate any other disease manifestation. We retrospectively looked at a group of seropositive NMOSD patients with brainstem symptoms to analyze disability during the course of the disease. We compared disability scores in patients who presented with those who did not present area postrema syndrome.

Material e Método / Material and method: We retrospectively studied selected patients examined at CIEM MS Research Center in Belo Horizonte, Brazil who met Wingerchuk's revised criteria for NMO and had their sera tested positive for anti-AQP4 IgG by indirect immunofluorescence or cell-based assays. Disability was assessed by the Kurtzke Disability Status Scale (EDSS) at each visit during the disease course. We divided patients according to duration of their disease into three groups: Group I. Duration < 5 years; Group II. Duration 5-20 years; Group III. Duration > 20 years. For each Group we compared patients who presented APS with those who did not have a history of APS. t-Student was used for statistical analysis.

Resultados / Results: The cohort comprised 68 AQP4-IgG seropositive NMOSD patients who presented signs of brainstem involvement. The number of patients in each Group according to the positive or negative history of occurrence of APS was as follows: Group I: 16 and 6; Group II: 25 and 13; Group III: 5 and 3. The median EDSS scores for each Group were 5.25 and 6.5; 6.0 and 6.0; 6.0 and 8.5. There were no significant differences in the intra-groups EDSS scores, independently whether patients had a positive or negative history of APS.

Discussão e Conclusões / Discussion and Conclusions: Severe disability tend to occur in AQP4-IgG seropositive NMOSD patients with brain stem involvement. Severity of disability, however, is not related to specific involvement of the dorsal medulla that results in APS. Acknowledgments: We thank Prof. K. Fujihara and Dr. D. Sato for help with the AQP4-IgG cell-based assay.

Palavras Chave / Key-Words: Neuromyelitis optica spectrum disorders; anti-aquaporin 4-antibody; area postrema syndrome; brainstem symptoms; disability.

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Data / Date: 2015-08-21

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Sala / Room: Auditorium

Forma de Apresentação / Presentation: POSTER

Autores / Authors: Vidal, C M , Macci, J P , Xavier, M F , Guedes, V R , Dias, J C , da Silveira, R C , Machiarullo, L N , Cal, H d S R , Dib, J G F , Nascimento, O J M , Matta, A P d C

Instituições / Institutions: Universidade Federal Fluminense - Rio de Janeiro - Brasil

Título / Title: Neuroimaging in Brazilian NMO patients.

Introdução / Introduction: Neuromyelitis optica (NMO) is an autoimmune inflammatory demyelinating disease with predilection for the optic nerve and the spinal cord causing recurrent attacks of blindness and paralysis. Brain abnormalities may be present but they do not fulfill the MS criteria. The purpose of this study is to describe the brain and spinal cord abnormalities found in magnetic resonance imaging (MRI) in a brazilian population with the diagnosis of NMO.

Material e Método / Material and method: Cross sectional study of 24 patients attended at the Neuroimmunology service of the UniversitaryHospital Antonio Pedro. All patients were submitted to clinical, laboratory and neuroimaging study of the spinal cord and brain. They all fulfilled the Wingerchuck (2006) diagnostic criteria.

Resultados / Results: Our sample had a predominance of female sex (87,5%), caucasian (62,5%), age ranging from 20 to 50 years old (mean 35,68 years old). Twenty patients were submitted to a complete neuroimaging evaluation (cervical, thoracic spinal cord and brain). Cervical longitudinally extensive myelitis (LEM) were present in 11 patients (47,8%), eight had rostral involvement of the medulla. Five patients (21,7%) had LEM from the cervical until the thoracic spinal cord. Both cervical and thoracic LEM involvements, not with continuous lesions, were present in six patients (26%). Brain demyelinating abnormalities were present in 14 patients, medulla involvement in 10 patients, periventricular lesions in six, subcortical in five; optic nerve in four; cerebellum, corpus callosum and pons in three patients each; hypothallamus in two patiens; one with corona radiatainvolvement.

Discussão e Conclusões / Discussion and Conclusions: Lesions in other places rather than spinal cord and optic nerve are compatible with the diagnosis of NMO. Brain abnormalities in the MRI have a different distribution from MS lesions. There is still a lack of information if the cases with brain lesions have a more aggressive course than the NMO cases with no brain involvement.

Palavras Chave / Key-Words: NMO; MRI; LEM; Myelitis

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Horário / Time: 16:30:00 às 18:00:00

Sala / Room: Auditorium

Forma de Apresentação / Presentation: POSTER

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Instituições / Institutions: CIEM/ UFMG - Minas Gerais - Brasil

Título / Title: ASSOCIATION BETWEEN RETINAL NERVE FIBER LAYER AND QUALITY OF LIFE IN PATIENTS WITH OPTIC NEURITIS HISTORY

Introdução / Introduction: To assess the visual quality of life in patients with a past history of optic neuritis (ON), and to observe whether this parameter could be correlated to the findings of the thickness of retinal nerve fiber layer (RNFL), as measured by optical coherence tomography (OCT).

Material e Método / Material and method: The translated and validated 25-Item National Eye Institute Visual Function Questionnaire (VFQ-25) was used to assess the visual quality of life of 32 patients with chronic ON, defined as the last ON attack for at least three months. They were recruited from the CIEM (Centro de Investigação em Esclerose Múltipla de Minas Gerais) Clinics and were diagnosed as NMOSD (Neuromyelitis Optica Spectrum Disorder) or Chronic Relapsing Optic Neuritis (CRON). Those who met a diagnosis of MS (multiple sclerosis) were not included. OCT was used for assessing correlation with VFQ-25. A multivariable regression model was used to evaluate this association.

Resultados / Results: A P value of .01 or less was deemed statistically significant. A strong correlation was found with binocular RNFL thickness reduction and the quality of life assessed by VFQ-25.

Discussão e Conclusões / Discussion and Conclusions: In the present study, structural damage measured by change in RNFL thickness was associated with a decrease in quality of life, specially when affecting both eyes. OCT is an important tool to assess clinical parameters and also quality of life. The VFQ-25 scores found in this population were comparable with published patient cohorts with specific ocular diseases as cataracts and age-related macular degeneration (AMD), in line with poorer visual recovery observed following ON in NMOSD and CRON.

Palavras Chave / Key-Words: optic neuritis, ophthalmology, visual acuity, optic coherence tomography, quality of life

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Forma de Apresentação / Presentation: POSTER

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Título / Title: Myelitis after human papillomavirus vaccine

Introdução / Introduction: A few cases of central nervous system (CNS) inflammatory syndromes following human papillomavirus (HPV) vaccine have already been reported. This seems to be first report of such a case in Brazil, where a large HPV immunization campaign has been released recently.

Material e Método / Material and method: Case report

Resultados / Results: On November 2014, a 15-year-old girl was admitted to our hospital due to a 2-week history of weakness and burning pain on her lower limbs, which progressed to flaccid paraplegia, sensory loss under the level of T12, urinary retention and fecal incontinence. No precipitant factors other than recent HPV vaccine (two months before) were identified. She denied any previous episodes of CNS dysfunction. Her past medical history was significant for a well controlled systemic lupus erythematosus (LES) under therapy with prednisone and hydroxychloroquine. Cerebrospinal fluid analysis showed cell count within normal limits, elevated protein (106 mg/dL) and mildly elevated IgG index (0.71). Magnetic resonance imaging (MRI) of the spinal cord showed a longitudinally extensive transverse myelitis (from T8 to the conus medullaris) with gadolinium-enhancement; anti-AQP4 and anti-MOG antibodies were not available. She underwent a 6-day course of methylprednisolone (1g/day) pulse therapy, without any improvement. Then, she underwent cyclophosphamide (1g) pulse therapy and was started on rituximab with a very mild improvement. On March 2015, she underwent a second cycle of rituximab. Follow up MRI showed partial recovery of the previously described lesion. No additional neurological improvement had been seen until her last follow-up visit, on June 2015.

Discussão e Conclusões / Discussion and Conclusions: HPV vaccine was likely the precipitating factor for an autoimmune disorder. Given that a large HPV immunization program is currently ongoing in Brazil, this case aimed to draw attention to neurological conditions potentially associated with the HPV vaccine.

Palavras Chave / Key-Words: Longitudinally extensive transverse myelitis, myelitis, human papillomavirus vaccine, neuromyelitis optica

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Forma de Apresentação / Presentation: POSTER

Autores / Authors: Sousa, M W G , Aguiar, M S , Maria, P R S , Uribe, C H , Ferreira, M F , Tauil , C B , Dias, R M , Grippe, T C , Aguilar, A C R , Martins, T A C , DIas, M S , Guiotti, M G , Barbosa, A L

Instituições / Institutions: Hospital de Base do Distrito Federal - Distrito Federal - Brasil

Título / Title: Clinical Experience with Rituximab Treatment in Neuromyelitis Optica Disorder: Report of a Case Series

Introdução / Introduction: Neuromyelitis optica (NMO) is a rare immune-mediated chronic inflammatory disease of the central nervous system (CNS). Clinically, it presents with optic neuritis (ON) and myelitis, often characterized by poor or no recovery. So far, there is no study comparing efficacy of drugs in treatment. Rituximab (RTX), a monoclonal antibody that targets CD20 antigen expressed on the surface of lymphocytes has been widely used for the treatment of NMO. In this study, we aim to report the results of RTX treatment in patients with relapsing NMO or NMO spectrum disorder (NMOSD) in follow-up at the Hospital de Base-Distrito Federal–Brazil between 2012 to 2015

Material e Método / Material and method: Retrospective analysis of a case series of patients with relapsing NMO or NMOSD treated with RTX (2 infusions 1 g of RTX at a fixed interval of every 6 months). Analyzing annualized relapse rate (ARR), disability (Expanded Disability Status Scale score) before and after treatment of RTX

Resultados / Results: Analyzes 7 patients with NMO or NMOSD previously treated with azathioprine (mean usage time 30,7±9,0 months with time of follow up 17,9/patients-year) and later with RXT due to therapeutic failure or drug intolerance (mean usage time 14.4±2.6 months with time of follow up 8,4/patients-year). Six patients became relapse free after RTX treatment with a important reduction in ARR (rate preRTX vs posRTX ARR,0,8±0,1vs0.3±0,3/Z=-0.943,p=0.345), whereas 1 patient died characterized as “non-responder” based on the fact that RTX failed to delay further relapses (4 attacks in 21 months). In 85,7% patients, the disability was either improved or stabilized after RTX treatment (EDSS preRTX vs EDSS posRTX, 5,2±,07 vs 5,0±0,6, p=0,576)

Discussão e Conclusões / Discussion and Conclusions: Treatment with RTX seems to be effective in case of intolerance or failure to azatioprina leads to sustained clinical response with reduction of relapses and improved disability scores

Palavras Chave / Key-Words: Neuromyelitis optica; Rituximab

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Instituições / Institutions: Hospital de Base do Distrito Federal - Distrito Federal - Brasil

Título / Title: Optic Chiasmal Neuritis As A First Manifestation Of Neuromyelitis Optica Spectrum Disorder

Introdução / Introduction: Optic Chiasmal Neuritis (OCN) is an inflammatory demyelinating condition of probable autoimmune or infectious etiology. Uni or bilateral, recurrent optic neuritis are clinical features observed in patients with Neuromyelitis Optica (NMO) and NMO spectrum disorders (NMOSD). The involvement of the optic quiasm, detected in magnetic resonance (MRI), has been described to have a strong association with this condition. To report a case of OCN as the first manifestation of NMOSD

Material e Método / Material and method: Case

Resultados / Results: A 42 year old woman presented with progressive decrease in visual acuity of the left eye, evolving into contralateral involvement in 7 days with bilateral orbital pain. Initial evaluation showed bilaterally decreased visual acuity and temporal hemianopsia of the left eye. Laboratory tests, including rheumatologic and serologic tests for syphilis and HIV showed no abnormalities. The cerebrospinal fluid was acelular, contained normal level of protein and glucose and was negative for VDRL. Orbits MRI revealed thickening of the optic chiasm suggestive of optic quiasmal neuritis. Serum anti-aquaporin 4 antibody (NMO-IgG) was positive (1:160). The patient showed poor response to high doses of methylprednisolone. The patient was diagnosed with NMOSD, and treatment with azathioprine was started

Discussão e Conclusões / Discussion and Conclusions: OCN is a rare condition that can be idiopathic or secondary to infectious or inflammatory demyelinating diseases. NMO is characterized by recurrent, unilateral or bilateral optic neuritis, relapsing extensive transverse myelitis, and seropositivity for antibodies NMO-IgG, as a supporting criteria. NMOSD is characterized by recurrent optic neuritis, transverse myelitis or hypothalamic or brain stem disorders, usually associated with NMO-IgG +. In our case, an aggressive OCN, with poor response to intravenous corticosteroids treatment and NMO-IgG + illustrated a case of NMOSD

Palavras Chave / Key-Words: Optic Chiasmal Neuritis; Neuromyelitis Optica

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Instituições / Institutions: Universidade Federal Fluminense - Rio de Janeiro - Brasil

Título / Title: Association between NMO and other autoimmune diseases in Brazilian patients

Introdução / Introduction: Neuromyelitis optica (NMO) is an autoimmune inflammatory disease of the central nervous system. It is characterized by attacks of optic neuritis and longitudinally extensive myelitis. NMO is associated with an auto-antibody that targets aquaporin-4 channels (anti-NMO) and, in many cases, multiple other non-specific auto-antibodies. Moreover, in some cases there is a concomitance between NMO and other autoimmune diseases.

Material e Método / Material and method: Cross-sectional study of 24 consecutive patients from the Neuroimmunology Service of the Federal Fluminense University. They all fulfilled Wingerchuk criteria (2006). Besides a systematic anamnesis and routine blood exams, serological markers for other autoimmune diseases were studied: ANA, anti-DNA, Anti-SSa, anti-SSb, anti-Sm, anti-TPO, Anti-thyroglobulin, rheumathoid factor, anti-cardiolipin IgM and IgG, ANCA, anti-Ach receptor.

Resultados / Results: Our sample showed a predominance of women (87.5%) Caucasian (62.5%) subjects, with age at diagnosis between 5 and 75 years (mean 36.58 years). We found the following concomitant autoimmune diseases: Hashimoto's thyroiditis (n=3), thyroiditis of unknown etiology (n=1), diabetes mellitus type 1-DM1 (n=1), Myasthenia Gravis-MG (n=1) and Systemic Lupus Erythematosus-SLE (n=1). We also assessed the family history of these patients. Dermatomyositis (n=1), psoriasis (n=1), thyroiditis (n=1),vitiligo (n=1) and SLE (n=2) were present in first-degree relatives. Anti-NMO positivity was found in 9 patients (37.5%), of those 3 patients had an autoimmune comorbidity (DM1, Hashimoto's thyroiditis and MG), 2 patients had family history of an autoimmune disease (dermatomyositis and SLE) and 1 patient was seropositive for anti-SM, anti-DNA and ANA without fulfilling clinical criteria for any specific disease.

Discussão e Conclusões / Discussion and Conclusions: There is a close relationship between NMO and other autoimmune diseases. This emphasizes a susceptibility to autoimmunity among NMO patients.

Palavras Chave / Key-Words: Neuromyelitis optica, NMO, anti-NMO, autoimmunity

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Sala / Room: Auditorium

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Instituições / Institutions: Universidade Federal Fluminense - Rio de Janeiro - Brasil

Título / Title: Inaugural symptoms in NMO patients

Introdução / Introduction: Neuromyelitis optica (NMO) is an immune-mediatedinflammatory severe demyelinating disease with axonal damage and predilection for the optic nerve and the spinal cord causing recurrent attacks of blindness and paralysis. It can present a monophasic or multiphasic pattern. The aim of this study is to describe the predominance of different clinical manifestations in the first presentationof NMO in a Brazilian population.

Material e Método / Material and method: Cross sectional study of 24 patients referred to the Neuroimmunology service of Federal Fluminense University. All patients were submitted to clinical, laboratory and neuroimaging study of the spinal cord and brain. They all fulfilled the Wingerchuck (2006) diagnostic criteria.

Resultados / Results: Our sample had a predominance of female (87.5%), Brazilian-Caucasians(62.5%), and age ranging from 5 to 75 years old (mean 36.58 years old). The average age at disease onset was 33.11 years old. Symptoms of the first relapse in our sample included: isolated myelitis (41.8%), bilateral optic neuritis (BON) (33.3%), optic neuritis associated with myelitis (12.5%), unilateral optic neuritis (UON) (8.3%), anorexia and lethargy (4.1%). Twenty patients developed a multiphasic disease with at least a second relapse. Associated brainstem manifestations at the first relapse werepresent in six patients (25%): vomiting in five, hiccups in two; syncope, vertigo and seizures in one patient each. One patient developed VI and VII cranial nerve palsy with myelitis.

Discussão e Conclusões / Discussion and Conclusions: Isolated myelitis is the most predominant clinical finding in the first relapse, which is compatible with other studies. The second most common opening symptom was BON while in the current literature it is described that UON is more frequent. Brainstem syndromes were present in a quarter of our sample, although it is described as a rare manifestation.

Palavras Chave / Key-Words: Neuromyelitis optica, NMO, inaugural symptoms

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Instituições / Institutions: HUOL-UFRN - Rio Grande do Norte - Brasil

Título / Title: CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF NEUROMYELITIS OPTICA IN NORTHEAST BRAZIL: OBSERVATIONAL STUDY IN A UNIVERSITY CENTER.

Introdução / Introduction: Neuromyelitis Optica (NMO) is a rare inflammatory disease of the central nervous system. Its epidemiological aspects are scarce. Some patients do not comply the classical diagnostic criteria, but exhibit positive AQP4-IgG, therefore they are classified as NMO spectrum disorders (NMOSD). Recently, a new international consensus about the NMOSD diagnostic criteria was published. The objective of this study is to present our data using the new criteria.

Material e Método / Material and method: Observational retrospective study from Hospital Universitário Onofre Lopes – UFRN database, from January 2001 to June 2015. NMO was diagnosed according to Wingerchuck et al. 2006 criteria and NMOSD according to Wingerchuk et al. 2015. We performed descriptive analysis and compared the means and frequencies between NMO and NMOSD groups.

Resultados / Results: 22 patients were analyzed, which 16 (72.2%) were NMO, 3 (13.6%) were NMOSD without AQP4-IgG and 3 (13.6%) were NMOSD with AQP4-IgG. In the general group, 17 (77.2%) were female and 5 (22.8%) were male. Mean age of 38.09 years old (SD 14). Mean outbreaks of 2.188 (SD 1.14). In the NMO group, 5 (31.2%) had monophasic disease and 11 (68.7%) presented themselves as relapsing cases. There was no statistical significance between NMO and NMOSD concerning age (p=0.5284), gender (p=0.5853) or number of outbreaks (p=0.5182). In the NMOSD group, all the males were AQP4-IgG negative. Treatment of acute exacerbation: methylprednisolone 1g intravenous in 22 patients (100%), plasmapheresis in 7 (31.8%), Immunoglobulin in 4 (18.2%). Attack prevention: Azathioprine in 16 patients (72.7%), Methotrexate in 2 (9.1%) and Rituximab in 7 (31.8%).

Discussão e Conclusões / Discussion and Conclusions: The new NMOSD classification allows the inclusion of patients without AQP4-IgG, who could not be diagnosed before. In our sample, NMO and NMOSD had mean age of outset around fourth decade and prevailed in females. NMOSD without AQP4-IgG predominated

Palavras Chave / Key-Words: Neuromyelitis Optica, NMO spectrum disorders, epidemiology

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Instituições / Institutions: HOSPITAL DAS CLÍNICAS DA FACULDADE DE MEDICINA DA UNIVERSIDADE DE SÃO PAULO - Sao Paulo - Brasil

Título / Title: Neuromyelitis optica and a peculiar vasculitis, a case report

Introdução / Introduction: Neuromyelitis optica (NMO) is a rare relapsing auto-immune disease of the central nervous system which is sometimes found in association with other autoimmune disorders. The overlap between NMO and another auto-imune diseases is frequent. In this report, the purpose is describe a patient with NMO confirmed by anti-aquaporina-4 antibody, followed after years by a medium artery's vasculitis of rigth hemibody and a episode of stroke.

Material e Método / Material and method: This case was evaluated with brain magnetic resonance imaging (MRI), cerebrospinal (CSF) analysis, and laboratory evaluation.

Resultados / Results: In december 2002 a 40-year-old woman sought treatment for an acute episode of severe transverse myellitis thad led paraplegia and weakness of left arm. MRI showed T2-weighted hyperintensity from C6 to T1 and postcontrast enhacement. The patient received intravenous methylprednisolone 1 gram for 5 days, with nearly complete recovery. After 4 months, the patient has a episode of bilateral retrobulbar optic neuritis, also treated with intravenous methylprednisolone 1 gram for 5 days, with complete recovery. Important CSF findings were 8 cells, and 4% eosinofils, with absence of oligoclonal igG bands. In december 2005 the patient was referred to our serrvice and was introduced azathioprine 150mg, with poor adherence. In 2006 and 2009 the patient presented news episodes of transverse myelitis, both with good recovery only with intravenous corticosteroids. Serum anti-aquaporin-4 antibody was positive (analysed by cell-based assays with live transfected cells). In 2010, the patient presented a necrotizing vasculitis on right arm and right leg, ANCA-negative, and with negative results for main-associated virus's vasculitis, without biopsy at the time, with spontaneous recovery. In 2015 the patient presents with stoke of the right posterior cerebral artery, of undertemined etiology after extensive research.

Discussão e Conclusões / Discussion and Conclusions: It is very important to recognize the relationship between autoimmune diseases and NMO. The association of Devic's disease with necrotizing vasculitis has not yet been described in the literature. A question is if this association is only casual or is a overlap of auto-imune diseases.

Palavras Chave / Key-Words: Neuromyelitis optica; Vasculitis

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Forma de Apresentação / Presentation: POSTER

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Instituições / Institutions: Hospital de Base do Distrito Federal - Distrito Federal - Brasil

Título / Title: Neuromyelitis Optica Spectrum Disorder with area postrema syndrome and diagnostic review: Case Report

Introdução / Introduction: Neuromyelitis Optica (NMO) is an autoimmune disorder characterized by severe optic neuritis and extensive transverse myelitis, as described in Wingerchuk diagnostic criteria. Recently, researches describe about the NMO spectrum disorder (NMOSD) that refers to the restricted form of the disease: optic neuritis or transverse myelitis recurrent or brain injury symptoms related to periventricular areas, both with or without positive anti-aquaporin4 (anti-AQP4). The case refers to a patient with NMOSD that had an area postrema syndrome with a positive anti-AQP4.

Material e Método / Material and method: Report a case of NMOSD with area postrema syndrome and diagnostic review.

Resultados / Results: Female, 22 years old, that presented incoercible vomiting and diplopia on 06/12/2014. The patient was evaluated by the Medical Clinic and released with advice to look for the Psychiatry on suspicion of conversion disorder to be, then, evaluated by the Neurology and referred for diagnostic investigation on 07/01/2014. During the clinical examination, it was detected the one and a half syndrome, nausea, vomiting and incoercible hiccups. MRI brain showed a demyelinating lesion in periaqueductal region and brainstem without highlighted contrast and brightness in the diffusion sequence. It was chosen to corticosteroid therapy with Methylprednisolone, with symptoms improvement, but still with diplopia. She took Prednisone during 3 months and had asymptomatic development. After three months without corticosteroids, it was collected a new anti-AQP4, reagent (1/160), different from the initial collected during the corticoscorticosteroid effect. Azathioprine was initiated.

Discussão e Conclusões / Discussion and Conclusions: The patient presented NMOSD with area postrema syndrome and without clinical criteria. Due to it is a disorder with poor prognosis, the clinical criteria needs to be revised for greater sensitivity in diagnosis and immunossuppressive therapy early introduction.

Palavras Chave / Key-Words: NMO, NMOSD, area postrema syndrome

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Forma de Apresentação / Presentation: POSTER

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Instituições / Institutions: Brazilian Committee for Treatment and Research in Multiple Sclerosis (BCTRIMS) - Minas Gerais - Brasil

Título / Title: PREVALENCE OF MULTIPLE SCLEROSIS IN ARAGUARI, SOUTHEASTERN BRAZIL

Introdução / Introduction: The prevalence of multiple sclerosis (MS) varies in different geographical areas and ethnic groups. Brazil extends over a large area and has a population with different racial backgrounds. As MS prevalence remains largely unknown in most parts of the country, the Brazilian Committee for Treatment and Research in Multiple Sclerosis (BCTRIMS) has launched a study to determine MS prevalence rate in the most representative cities of Brazil as distinct geographical and racial aspects are concerned. In this study the targeted cities were then named “key-geographical cities”.

Material e Método / Material and method: OBJECTIVE: Herein we describe the findings of MS prevalence in Araguari, State of Minas Gerais, in southeastern Brazil, the first of the key-geographical cities selected in the BCTRIMS MS prevalence study. METHODS: The geographical, demographic and economic activities data on Araguari were obtained from IBGE. The prevalence day was July 1, 2012 as the population of Brazilian cities has been established for this date. Two neurologists from different participant MS Centers took the history from pre-selected patient and checked their physical examination, CSF analysis results and brain and spinal MRI. Only patients who met McDonald’s (2005) diagnostic criteria for MS were included. The clinical forms of the disease were defined according to consensus criteria established by Lublin et al. (2006). Patients’ disability scores were classified according to Kurtzke’s EDSS.

Resultados / Results: The city of Araguari is situated in the state of Minas Gerais, southeastern Brazil, has an area of 2,731 Km2, elevation of 1,013 m, and a population of 109,801 inhabitants. Eighteen MS patients were identified and 17 were reviewed (13 females; 15 Whites and 2 Mulattoes) were identified in the city. Median age at disease onset was 32 (18-54) years.

Discussão e Conclusões / Discussion and Conclusions: Multiple sclerosis prevalence in Araguari is 17x10-5. This rate is similar to those previously reported in other Brazilian southeastern cities.

Palavras Chave / Key-Words: Key-Words: Multiple sclerosis; prevalence study; Araguari; BCTRIMS Acknowledgments: This study was supported by an unrestricted grant by Novartis.

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Instituições / Institutions: CIEM MS Research Center - Minas Gerais - Brasil

Título / Title: BRAINSTEM SYNDROME AS THE INITIAL MANIFESTATION OF NEUROMYELITIS OPTICA SPECTRUM DISORDER

Introdução / Introduction: Although optic neuritis and transverse myelitis are the most common manifestations of neuromyelitis optica spectrum disorders (NMOSD) symptoms related to brainstem involvement were recognized since the early descriptions of the disease. Brainstem symptoms (BSS) may occur in any phase during the course of the disease, and are usually associated with signs of visual or spinal cord abnormalities. Interestingly, some NMOSD patients develop isolated BSS as the inaugural manifestation of the disease, preceding both optic neuritis and transverse myelitis. OBJECTIVE: To analyze the demographic and clinical characteristics of the NMOSD patients who had BSS at different phases during the course of the disease.

Material e Método / Material and method: We reviewed the medical records of patients examined at CIEM MS Research Center in Belo Horizonte, Brazil, who met the revised 2006 diagnostic criteria for neuromyelitis optica and Wingerchuk's definition of NMOSD (2007). Serum anti-aquaporin 4 antibody was tested by indirect immunofluorescence or cell-based assay at Tohoku University, Japan. Patients with BSS were divided into groups according the phase of development and characteristics of the symptoms.

Resultados / Results: We identified 55 NMOSD patients in whom BSS occurred as an isolated phenomenon at the disease onset. Out of these 55 patients, 50 were females, 18 Whites, 23 Mulattoes, 13 Blacks and 1 Asian. The median age at disease onset was 30 (3-64) years. Anti-AQP4 IgG serostatus was positive in 34 patients, negative in 12, and not assessed in 9. Intractable nausea/vomiting and hiccups were the most frequent symptoms, occurring in 34 (61.8%) patients, whereas dizziness was observed by 13 (23.6%) and diplopia by 12 (21.8%).

Discussão e Conclusões / Discussion and Conclusions: Brainstem symptoms may herald more commonly observed NMOSD manifestations as optic neuritis and transverse myelitis. Clinicians should include NMOSD in the differential diagnosis of isolated brainstem syndrome, use sensitive assays to detect serum AQP4-IgG, establish the correct diagnosis and promptly start prophylactic treatment to decrease the risk of severe neurologic disability. Acknowledgments: We thank Prof. K. Fujihara and Dr. D. Sato for help with the AQP4-IgG cell-based assay.

Palavras Chave / Key-Words: Neuromyelitis optica spectrum disorders; anti-aquaporin 4-IgG; brainstem symptoms

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Instituições / Institutions: CIEM MS Research Center, Federal University of Minas Gerais Medical School - Minas Gerais - Brasil

Título / Title: CARDIAC ARRHYTHMIA IN ANTI-MOG IGG SEROPOSITIVE PATIENT WITH PHENOTYPE OF NEUROMYELITIS OPTICA SPECTRUM DISORDER

Introdução / Introduction: Recently antibodies to myelin oligodendrocyte glycoprotein (anti-MOG) were identified in the serum of a small group of patients who meet diagnosis for neuromyelitis optica spectrum disorders (NMOSD). The exact relationship of these patients with the more characteristic group of patients with anti-aquaporin 4 (anti-AQP4) autoimmunity remains to be clarified. The dorsomedial hypothalamus (DMH) plays a key role in integrating cardiovascular responses to stress. There is also a positive relationship between midbrain activity and potentially proarrhythmic abnormalities in ventricular repolarization during psychological and physical stress.

Material e Método / Material and method: OBJECTIVE: To describe a case of paroxysmal ventricular tachycardia occurring in a young male who developed unilateral optic neuritis and was then found to be anti-AQP4 antibody seronegative and anti-MOG antibody seropositive.

Resultados / Results: CASE REPORT: A 15-year-old mulattoe male presented with fatigue, shortness of breath and chest discomfort during exercise. An EKG demonstrated monomorphic paroxysmal ventricular tachycardia. He underwent cardiovascular work-up including echocardiography, holter, and heart MRI that yielded normal results. An Implantable Cardioverter Defibrillator (ICD) was placed to monitor and control the heart rate. Two months later, he developed severe left optic neuritis, underwent IV pulses of methyllprednisolone, and had partial recovery. Past history and family history were negative. Laboratory work-up was unrevealing including cell-based assay for anti-AQP4 IgG. However, test for anti-MOG IgG yielded positive result. Skull CT scans and cerebrospinal fluid analysis were normal. Brain and spinal MRI were not done (because of the implanted defibrillator and lack of consent by patient's family). The patient was put on azathioprine and had no further attack.

Discussão e Conclusões / Discussion and Conclusions: CONCLUSION: The association of cardiac arrhythmia of unknown cause with severe optic neuritis prompted the diagnostic hypothesis of NMOSD. Serology for AQP4 IgG was negative but for anti-MOG IgG was positive. It is probable that cardiac arrhythmia resulted from diencephalic or midbrain involvement. Descriptions of abnormalities occurring in anti-MOG IgG seropositive patients, such in the present report, may shed some light in the pathogenesis of the NMOSD.

Palavras Chave / Key-Words: KEY-WORDS: Cardiac arrhythmia; neuromyelitis optica spectrum disorders; anti-aquaporin 4-antibody; anti-myelin oligodendrocyte glycoprotein antibody; optic neuritis Acknowledgments We thank Prof. K. Fujihara and Dr. D. Sato for help with the AQP4-IgG cell-based and anti-MOG-IgG assays.

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Autores / Authors: Fonseca da Silva, S C , Talim, N C , Freitas, H , Kleinpaul, R , Amaral, J M S S , Talim, L E C , Lana-Peixoto, M A

Instituições / Institutions: CIEM MS Research Center, Federal University of Minas Gerais Medical School - Minas Gerais - Brasil

Título / Title: MULTIPLE SCLEROSIS DEVELOPING IN PATIENT WITH AUTOIMMUNE HEPATITIS

Introdução / Introduction: Although liver dysfunction most commonly occurs in multiple sclerosis (MS) patients due to adverse effects of disease-modifying-therapy, neurologists are to be aware that it may also derive from direct autoimmune damage. Autoimmune hepatitis (AH) is a chronic inflammation of the liver that affects children and adults. It may be associated with a variety of conditions such as thyroiditis, myasthenia gravis and rheumatoid arthritis. The association of AH and MS is rare and usually occurs in patients under treatment with immunomodulatory drugs or steroids which may act as trigger agents. Herein we report a young patient who presented AH and 24 years later developed MS. To our knowledge MS development after AH for such a long interval has not been reported in the literature.

Material e Método / Material and method: .

Resultados / Results: CASE REPORT A 51-year-old white female was referred to CIEM MS Research Center with history of recurrent optic neuritis in the right eye with gait ataxia. She had had an episode of simultaneous bilateral optic neuritis with full recovery seven months earlier, and bursts of sensory disturbances in the lower limbs that started at the age of 42. She had a past history of hepatitis at age of 16 characterized by lethargy, malaise, abdominal pain, arthralgia, jaundice and liver dysfunction tests. Infectious hepatitis was ruled out and diagnosis of AH was confirmed by serology and biopsy. Complete serological tests revealed positive anti-smooth muscle antibodies, positive anti-nuclear antibodies, and negative liver kidney microsomal antibodies. Liver biopsy showed lobular lymphoplasmocytic infiltrate associated with some eosinophils. The patient was started on prednisone and azathioprine with good therapeutic response. Family history was significant as the patient had two sisters with MS. Brain MRI showed large cavitary lesions in periventricular regions, small lesions in the corpus callosum, deep white matter and pons-mesencephalic transition. Spinal MRI disclosed T2-hyperintensive lesions in C3-C4 and C6-C7. Cerebrospinal fluid IgG index was 2.3. Cell-based assay for detection of serum AQP4 –IgG was negative.

Discussão e Conclusões / Discussion and Conclusions: The present case shows a unique feature as compared with previous reports of the association of MS and AH. Our patient developed MS long after having had AH. The underlying mechanisms that link these two conditions remain unclear.

Palavras Chave / Key-Words: Key-Words: Multiple sclerosis, autoimmune hepatitis, autoimmunity Acknowledgments: We thank Prof. K. Fujihara and Dr. D. Sato for help with the AQP4-IgG cell-based assay.

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Instituições / Institutions: CIEM MS Research Center - Minas Gerais - Brasil

Título / Title: NEUROMYELITIS OPTICA SPECTRUM DISORDERS IN PATIENTS UNDER 18 YEARS: ANALYSIS OF 10 CASES

Introdução / Introduction: There are few international series describing neuromyelitis optica spectrum disorders (NMOSD) in children and most of them emphasize their similar features to those occurring in adult patients. On the other hand they also call attention to some differential aspects which make them more similar to acute disseminate encephalomyelitis (ADEM). We looked at the demographic and clinical features of children with NMOSD examined at CIEM MS Research Center in Belo Horizonte, Brazil, in order to better characterize the disease in this age group.

Material e Método / Material and method: We reviewed the medical records of all patients who met Wingerchuk's 2006 revised diagnostic criteria and 2007 definition of NMOSD and whose inaugural manifestation of the disease occurred at age of 18 years or before. Disability was assessed by the Kurtzke Disability Status Scale (EDSS) at each visit during the disease course.

Resultados / Results: Ten children meeting criteria for diagnosis of NMOSD were identified. There were 9 females; median age at disease onset was 13.5 (5-18) years. Two children developed longitudinally extensive transverse myelitis (LETM), 3 had optic neuritis (ON), 2 combined transverse myelitis and optic neuritis, and 3 area postrema syndrome. AQP4-IgG seropositive status was found in 6 out of the 10 children had had seropositive statushad the relapsing form of NMOSD. AQP4-IgG seropositive status was found in 6 out of 8 children. The median EDSS was 4.5 (1.5 – 8.5). Brain MRI was abnormal in 6 patients. Spinal MRI disclosed longitudinally extensive centromedullary lesions which involve the cervical spine in 9 cases and thoracic spine in 7.

Discussão e Conclusões / Discussion and Conclusions: Our series is similar to other previously reported by other authors, showing that NMOSD in children are mostly alike those occurring in adults. Physicians, however, are to be aware of the differential diagnosis with other demyelinating diseases of childhood. Acknowledgments We thank Prof. K. Fujihara and Dr. D. Sato for help with the AQP4-IgG cell-based assay.

Palavras Chave / Key-Words: Neuromyelitis optica spectrum disorders in children; anti-aquaporin 4-antibody; optic neuritis; transverse myelitis

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Instituições / Institutions: CIEM MS Research Center - Minas Gerais - Brasil

Título / Title: NEUROMYELITIS OPTICA SPECTRUM DISORDERS IN THE ELDERLY

Introdução / Introduction: Neuromyelitis optica spectrum disorders (NMOSD) comprise a group of frequently disabling disorders that more commonly results from attacks of specific autoantibodies to sites with high expression of aquaporin-4 in the central nervous system. Although the disease has been described in all age groups, disease onset most frequently occurs around 40 years. Onset in the elderly has seldom been reported.

Material e Método / Material and method: We reviewed the medical records of all patients diagnosed with NMOSD at CIEM MS Research Center in Belo Horizonte, Brazil, to identify patients whose inaugural manifestation of the disease occurred at age 60 or older. For diagnosis of NMOSD Wingerchuk's 2006 revised diagnostic criteria and 2007 definition of NMOSD were used. Disability was assessed by the Kurtzke Disability Status Scale (EDSS) at each visit during the disease course.

Resultados / Results: We identified seven patients who met the diagnostic criteria and who were 60 years of age or older at disease onset. There were five males; the median age at disease onset was 67 (61-78) years. The initial event was transverse myelitis in 5 and bilateral simultaneous optic neuritis in 2. Two patients had monophasic NMOSD. The median EDSS was 7.5 (4.5-10). All patients were AQP4-IgG seropositive and had abnormal brain MRI. Spinal MRI disclosed lesions in the cervical cord in five patients and in the thoracic cord in 4.

Discussão e Conclusões / Discussion and Conclusions: Review of our NMOSD patients with AQP4-IgG seropositive status whose disease starts at old age suggest that in this age group the NMOSD predominate in males, affect more frequently the spinal cord than the optic nerves and may have a more severe outcome. As this series is small a multicenter study is warranted to better characterize the clinical features of the disease in the elderly.

Palavras Chave / Key-Words: Neuromyelitis optica spectrum disorders; anti-aquaporin 4-antibody; optic neuritis; transverse myelitis, elderly

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Instituições / Institutions: Universidade Federal Fluminense - Rio de Janeiro - Brasil

Título / Title: The relevance of anti-aquaporin 4 status in Brazil NMO patients

Introdução / Introduction: Neuromyelitis optica(NMO) is a monophasic or recurrent inflammatory autoimmune disease of the central nervous system that usually presents as relapses of optic neuritis(ON) and myelitis(ML). Anti-aquaporin 4 antibody(also known as anti-NMO) is considered a major biomarker for the disease and its presence allows early and appropriate diagnosis.

Material e Método / Material and method: Retrospective study of 24 patients followed in the Neuroimmunology Service of the Federal Fluminense University, Rio de Janeiro, Brazil. Anti-NMO status was detected by indirect immunofluorescence (IFI). They all fulfilled Wingerchuk criteria (2006).

Resultados / Results: Average age was 36.58 years-old, most of them women (87.5%), and caucasian(62.5%). Anti-NMO seropositivity was found in 37.5% of the sample, being 19.7% female and 5.3% male. Four patients (12.5%) were not tested for this antibody. The average age of disease onset was 33.11 years-old. We found a total number of relapses of 3.5 per patient and EDSS score of 7 among anti-NMO positive subjects, and respectively 2.5 ($p=0.05$) and 5 ($p=0.25$) among those negatives, taking into account similar follow-up periods. Among the whole sample, inaugural relapses were different between patients, as follows: isolated ML (41.8%), bilateral ON (33.3%), ON associated with ML(12.5%), unilateral ON (8.3%), anorexia and lethargy (4.1%). There were no statistically diference between the two groups ($p>0.05$). All seropositive subjects had a recurrent disease, while four (26.6%) seronegative subjects had monophasic NMO. Other associated symptoms were vomiting (20.8%), hiccups (12.5%), dizziness (12.5%), seizure (4.1%) and facial and abducens nerves palsy(4.1%) .

Discussão e Conclusões / Discussion and Conclusions: Despite the small sample and the low sensibility of IFI, the main limitations of our study, we found a trend to a higher number of relapses and EDSS score among seropositive patients. Seronegative patients were more prone to have a monophasic course.

Palavras Chave / Key-Words: Neuromyelitis optica, anti-aquaporin 4

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Autores / Authors: Saad, T R , Penna e Costa, A A , Santa Ignês, L J , Monteiro, M C , Mayrink, L , Magalhães, E S , Vasconcelos, Z , de Souza, A , de Azedevo, L

Instituições / Institutions: Instituto Fernandes Figueira - FIOCRUZ - Rio de Janeiro - Brasil

Título / Title: STRIVING FOR THE BEST TREATMENT FOR PEDIATRIC ACUTE DEMYELINATING SYNDROMES: RESULTS FROM COHORT ANALYSIS

Introdução / Introduction: The 2013 International Pediatric MS Study Group report brings awareness to the difficulties in managing the diagnostic work-up and treatment of Pediatric Acute Demyelinating Syndromes (ADS), and highlights their differences from adult onset forms and the need for pediatric guidelines. Taking into account that pediatric ADS course with increased inflammatory response, frequent relapses, long term disabilities and quality of life losses, a specialized outpatient clinic to follow-up children with ADS was created in our hospital. Cohort analysis of these patients and work-up/therapeutic strategies are described in this study.

Material e Método / Material and method: Prospective cohort analysis from a Pediatric ADS clinic population over the past year.

Resultados / Results: Eighteen patients (8 boys), mean age of 7.3yo (range: 1.8-13yo), at their first episode of ADS were seen in clinic, and protocols were created to be used through their differential diagnosis, relapses and remission phases. Five presented with multiple sclerosis (MS), 7 with Acute Disseminated Encephalomyelitis (ADEM), 3 with Neuromyelitis Optica (NMO), and 3 with Clinically Isolated Syndromes. Seven patients presented ADS symptoms prior to temporal-spatial dissemination diagnosis. Serum from all patients were tested for inflammatory biomarkers: IgG index calculation, oligoclonal Bands, lymphocyte counts, cytokines (IFN-gamma, TNF-alpha, IL-17, IL-4 and IL-10). Currently, five patients with MS are treated with subcutaneous Interferon beta-1A, and a fourth with Glatiramer acetate due to prior treatment failure. NMO is treated with Azathioprine or Glatiramer acetate. Immunotherapy/cyclophosphamide treatment is used for ADEM with good response.

Discussão e Conclusões / Discussion and Conclusions: This preliminary cohort analysis describes our current work-up and therapeutic protocols for ADS at our hospital.

Palavras Chave / Key-Words: Acute Demyelinating Syndromes, Pediatric,cohort analysis

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Autores / Authors: Pereira, W L C J , Voltarelli, M , Alfieri, D F , Flauzino, T , Kallaur, A P , Martins, G G , de Moura, L A , Simão, A N C , Kaimen-Maciel, D R , Reiche, E M V

Instituições / Institutions: Universidade Estadual de Londrina - Parana - Brasil

Título / Title: Association between chemokine receptor 5 Δ32 deletion (rs333) with the disability of patients with neuromyelitis optica

Introdução / Introduction: NMO etiology is multifactorial. The chemokine receptor 5 (CCR5) plays an important role in the inflammatory response in demyelinating diseases and genetic variations in CCR5 can alter the immune response. The aim of this study was to associate the delta 32 polymorphism (rs333) of CCR5 (CCR5Δ32) with susceptibility to NMO and with disability of patients with NMO treated in Londrina and region.

Material e Método / Material and method: In a case-control, 22 patients were included consecutively in the 12-month period, from the Outpatient Neurology Clinic of the Specialties Hospital of the State University of Londrina, Londrina, Paraná. Neurological disability was assessed with the EDSS. As controls, 50 healthy individuals were consecutively selected blood donors of the Regional Blood Center of Londrina. The genotyping of CCR5 delta 32 was performed using genomic DNA extracted from peripheral blood leukocytes and a fragment of 225 base-pairs of CCR5 was amplified by polymerase chain reaction.

Resultados / Results: Of the 22 patients, 21 (95.5 %%) were female; the median age was 44.5 years (IQR 33.0 to 51.3) and 21 (95.5%) had relapsing NMO. The median age of disease onset was 36.0 years (IQR 26.0 to 44.3) and the EDSS was 4.3 (IQR 3.5 to 5.3). Of the 22 patients, 12 (54.5%) had anti-aquaporin 4 antibodies (p = 0.2628). No significant differences were found in the genotypic and allelic frequency between patients and controls. CCR5/CCR5 and CCR5/CCR5Δ32 genotypes were observed in 20 (90.1%) and 2 (9.9%) patients, respectively, and 127 (96.2%) and 5 (3.8%) controls, respectively (p = 0.2621). Association between genotypes and the clinical and immunologic characteristics of patient evaluated was not observed (p> 0.05). An association was observed between the CCR5/CCR5Δ32 and the EDSS (p=0.0390).

Discussão e Conclusões / Discussion and Conclusions: The results may contribute to a better understanding of the pathophysiology of NMO.

Palavras Chave / Key-Words: Neuromyelitis optica, chemokine receptor 5, genetic polymorphism, CCR5Δ32, disability

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Autores / Authors: Pereira, W L C J , Kallaur , A P , Oliveira, S R , Simão , A N C , Lozovoy, M A B , Alfieri, D F , Flauzino, T , Grotti, D M , Reiche, E M V , Kaimen-Maciel, D R

Instituições / Institutions: Universidade Estadual de Londrina - Parana - Brasil

Título / Title: FREQUENCY OF AUTOIMMUNE DISORDERS AND AUTOANTIBODIES IN PATIENTS WITH NEUROMYELITIS OPTICA FROM SOUTHERN BRAZIL USING DIFFERENT DOSES OF PREDNISONE

Introdução / Introduction: Neuromyelitis optica (NMO) is associated with the presence of other autoimmune disorders and multiple autoantibodies.

Material e Método / Material and method: Twenty two patients with NMO diagnosed according to the 2006 diagnostic criteria were included. Demographic and clinical data were obtained using a standard questionnaire and from medical records. The disability was evaluated using the EDSS. All the patients were treated with prednisone in combination with other immunosuppressive drugs (azathioprine or mycophenolato mofetil). The patients were divided in two groups: 13 patients treated with 10 mg/day of prednisone (group 1), and 9 patients treated with >10 mg/day of prednisone (group 2). The serum autoantibodies evaluated were anti-AQP4, TRAb, ANA, anti-TPO, anti-Tg, ANCA, anti-CCP, rheumatoid factor, anti-SSA/Ro, anti-SSB/La, anti-Sm, anti-RNP, anti-nucleosome, and anti-Scl70. TSH and free T4 were also measured.

Resultados / Results: The frequency of women (95.5%) was higher than men (4.5%), and the median age of disease onset and median disease duration were higher among the group 1 than group 2 (48.5 vs 37.0 years; p=0.0482; 7.0 vs 2 years, p=0.0240, respectively). Six (27.3%) patients presented NMO associated with other autoimmune disorders, such as Hashimoto thyroiditis (n=2), Graves' disease (n=1), juvenile rheumatoid arthritis (n=1), systemic lupus erythematosus and systemic sclerosis (n=1), and Raynaud's phenomenon (n=1).The most frequent autoantibodies detected were anti-AQP4 in 12 (54.5%) patients, anti-nucleosome in 7 (31.8%), ANA in 6 (27.3%), anti-TPO in 6 (27.3%), and anti-Tg in 5 (22.7%) patients.

Discussão e Conclusões / Discussion and Conclusions: The study underscores the high frequency of autoimmune disorders and autoantibodies in patients with NMO. Further studies with large number of NMO patients may contribute to advances in the understanding of NMO disease mechanisms.

Palavras Chave / Key-Words: neuromyelitis optica, Devic's disease, autoimmunity, aquaporin 4, autoantibodies

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Autores / Authors: Pereira, W L C J , Reiche, E M V , Kallaur , A P , Kaimen-Maciel, D R

Instituições / Institutions: Universidade Estadual de Londrina - Parana - Brasil

Título / Title: Immunopathological mechanisms involved in the neuronal damage of patients with neuromyelitis optica: a review

Introdução / Introduction: The aim of this study was to review the immunopathological mechanisms involved in the neuronal damage of patients with neuromyelitis optica (NMO).

Material e Método / Material and method: It was made a review of published papers until 2014.

Resultados / Results: In the periphery, environmental factors, such as virus and bacteria, induce an innate immune response and activated microglia presents antigens to the adaptive immune response with activation of Th1, Th2, and Th17 cells. Th1 and Th17 secrete inflammatory cytokines, such as IFN-γ and IL-17, respectively, which activate other inflammatory cells and amplify the innate immune response; and Th2 secrete IL-10 that modulates Th1. These cells express different chemokine receptors that contribute to the recruitment of other inflammatory cells to the CNS. NMO pathogenesis involves binding of anti-AQP4 to AQP4 on astrocyte end-feet that causes antibody-dependent cellular cytotoxicity (ADCC) when effector cells are present, such as neutrophils, eosinophils, and natural killer cells, and complement-dependent cytotoxicity (CDC) when complement is present. These events are followed by recruitment of inflammatory cells, first neutrophils and eosinophils (granulocytes), and then macrophages, which disrupt the blood-brain barrier (BBB), allowing more entry of anti-AQP4 IgG. Degranulating inflammatory cells and astrocytes damage secondarily cause oligodendrocytes injury, myelin loss, and axon damage by ADCC. NMO pathogenesis also involves glutamate excitotoxicity by a mechanism involving anti-AQP4 IgG-induced internalization of glutamate transporter excitatory amino acid transporter 2 (EEAT2) on astrocytes and consequent injury in glutamate uptake from the extracellular space following neuroexcitation.

Discussão e Conclusões / Discussion and Conclusions: More advances in the understanding of NMO disease mechanisms are needed.

Palavras Chave / Key-Words: neuromyelitis optica; aquaporin 4 antibodies; cytotoxicity; autoimmunity; optic nerve; spinal cord