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Neuromuscular Disorders 1

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Neuromuscular Disorders 1
Clinical and serological investigation of IGM paraproteinemic neuropathies without anti-MAG antibody activities

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Background: About half of the patients with IgM paraproteinemic neuropathies have IgM M-proteins reactive with myelin-associated glycoprotein (MAG). Few studies have been reported on the clinical and serological features of anti-MAG-negative IgM paraproteinemic neuropathies.
Objective: To investigate clinical and serological characteristics of anti-MAG-negative IgM paraproteinemic neuropathies.
Patients and methods: We investigated 33 patients with IgM paraproteinemic neuropathies without anti-MAG antibody activities. We examined IgM antibody activities of the sera from those patients by using ELISA, at the dilution of 1:40. Eight gangliosides (GM1, GM2, GM3, GD1a, GD1b, GD3, GT1b and GQ1b) were used as antigens. The study was approved by IRB of the university.
Results: Among the 33 patients, thirteen patients had anti-GM1 activities, 6 had activities to gangliosides with disialosyl residue (GD1b, GD3, GT1b and GQ1b), and 3 had activities to GD1b. When the antibody assay was performed at higher dilution (1:160 or 1:640), anti-GM1 activities were decreased whereas the activities of the antibodies to gangliosides with disialosyl residue or to GD1b (anti-disialosyl antibodies) were increased. Light chain types of anti-disialosyl antibodies were identical to those of IgM M-proteins, suggesting that IgM M-proteins had antibody activities. Among the 9 patients with anti-disialosyl antibodies, 8 had sensory ataxia. Seven patients with anti-disialosyl antibodies were treated with IVIg and 5 of them showed improvement.
Conclusion: About 25% of the patients with anti-MAG-negative IgM paraproteinemic neuropathies had common features; IgM M-protein with anti-disialosyl antibody activities, sensory ataxic neuropathy and relatively good response to IVIg.

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Neuromuscular Disorders 1
Association of other autoimmune diseases in patients with myasthenia gravis: Its frequency and characteristics

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Background & objective: Patients with myasthenia gravis (MG) occasionally accompany other autoimmune diseases which oblige immunomodulation. To improve their long-term management, we launched into summarization of its real frequency and characteristics.
Patients & methods: Medical charts of MG patients diagnosed and/or treated in our hospital between April 1995 and April 2015 were retrospectively reviewed.
Results: Ninety-six patients (age at onset, 2–87 years old/ disease year as MG at last follow-up, 1st–55th, median 5th) were identified, of which 31 were males and 65 females, 42 ocular and 54 systemic, 30 with thymoma (31%), 12 seronegative (13%; double-seronegative 5, positive MuSK 1). Other autoimmune diseases have been recognized before, at the time, or after presentation as MG in 26 cases (27%) who were all seropositive but one. They are Hashimoto disease (11 cases, one with encephalopathy), systemic lupus erythematosis (3), rheumatoid arthritis (2), nephrotic syndrome (2), and each single case of autoimmune Factor VIII deficiency, erythroderma, myocarditis, Graves disease, myocarditis, Graves disease, interstitial pneumonitis, polymyositis, adrenal insufficiency, vitamin B12 deficiency, autoimmune hepatitis, type 1 diabetes mellitus, antiphospholipid syndrome, primary biliary cirrhosis. Their occurrence seems not related to MG phenotype, patient's age or sex, or presence of thymoma. Except for 2 patients manifesting polymyositis or autoimmune hepatitis simultaneously with MG symptoms, activity of MG and other autoimmune diseases occurred at different times.
Conclusion: More than a quarter of MG patients complicate other autoimmune diseases in their life time. Therefore, in their long-term management, especially when with immunomodulative agents, constant attention should be paid to their systemic immunological status.

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Neuromuscular Disorders 1
Myotonic dystrophy type 1: Neuropsychological and brain magnetic resonance image study

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Objective. To characterize neuropsychological and neuroimaging profile in a cohort of Myotonic Dystrophy Type 1 (DM1) Brazilian patients.
Methods. A descriptive study encompassed 13 genetic proved DM1 patients compared to 14 controls with correction for gender, age and education. We performed: motor scale; Mini-Mental Examination;

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Beck depression inventory; Wechsler Adult Intelligence Scale (WAIS III); and a comprehensive neuropsychological examination (10 tests). MRI was done in a 2 Tesla scanner, using VBM and single voxel spectroscopy in three areas. Non-parametric statistical analysis was applied to cognitive and spectroscopy data and t-test with two independent samples to VBM data.

Results. In 6 DM1-infantile and 7 DM1-classical types the psychometric performance by WAIS III was worse on the verbal scale. It was found significant impairment of constructive visuospatial praxis with Kohs' blocs and the incongruent Stroop test, not correlated with motor performance in DM1. There was no significant difference in the other tests. VBM gray matter atrophy was found in patients in frontal regions, predominantly at right: inferior gyrus, orbicularis, triangular and opercular; pre-central gyrus; right parahippocampal gyrus and bilateral cingulate gyrus; middle and superior left temporal gyri. Atrophy of the white matter occurred in the posterior corpus callosum, medial frontal gyrus and medial temporal pole at right and uncus bilaterally. Temporoparietal N-acetyl aspartate was correlated with poorer performance on the Stroop test and atrophy of the left temporal gray matter.

Conclusion. The cortico-subcortical changes identified showed a relationship with the neurofunctional networks related to neuropsychological visuospatial constructive and executive inhibitory process.

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Neuromuscular Disorders 1
An overview of the demography, clinical characteristics and genetics of Latin America patients enrolled in THAOS

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Introduction: The natural course of transthyretin-related amyloidosis (ATTR) is poorly defined due to the heterogeneity in genotype and phenotype as well as the relatively low disease prevalence. The global, non-interventional THAOS (Transthyretin Amyloidosis Outcomes Survey) patient registry was established in 2007 to collect and analyze data on symptom occurrence and progression and on the effects of disease modifying treatments in a large, diverse patient population.*
Objective: This current analysis provides a Latin-American perspective on the THAOS dataset.
Patients and methods: THAOS is an ongoing, longitudinal, observational registry open to all symptomatic individuals with confirmed hereditary or acquired ATTR, as well as to asymptomatic carriers of known pathogenic *TTR* mutations. Patient data from a range of standard assessments are obtained during clinical evaluations and recorded using an interactive Web-based system.
Results: As of January 2015, a total of 2543 subjects from 17 different countries were enrolled in THAOS, with 81 different *TTR* genotypes. Three countries from Latin America participate in THAOS and registered total of 256 subjects (Argentina 51, Brazil 148, and Mexico 57). Most patients from Brazil (91.9%) and Argentina (96.1%) carried the Val30Met mutation, whereas the Ser50Arg mutation (80.7%) was predominant in Mexico. Majority of subjects from Latin America presented with neurologic phenotype, followed by subjects presented as mixed phenotype. 12.3% patients from Mexico presented as cardiologic phenotype.
Conclusions: The large dataset from the THAOS registry presents a unique opportunity to improve our understanding of the diverse presentations including the regional differences and the natural history of ATTR.

*IRB statement: All study sites obtained institutional and local review board approval prior to patient enrolment.

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Neuromuscular Disorders 1
THAOS – The Transthyretin Amyloidosis Outcomes Survey – Report on the patient demographic and baseline characteristics after 7 years of initiation

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Background: Transthyretin (TTR) amyloidosis is a rare, life-threatening, systemic condition with two main forms: hereditary (associated with TTR gene mutations) and wild-type (WT) amyloidosis. Established in 2007, the Transthyretin Amyloidosis Outcomes Survey (THAOS) is a comprehensive registry for TTR amyloidosis patients and asymptomatic carriers. This global, longitudinal, observational survey aims to document its natural history and the efficacy and safety of treatment modalities.
Objective: The present analysis describes baseline demographic and disease characteristic of subjects enrolled in the THAOS registry as of January 2015, 7 years after its initiation.*
Patients and methods: Symptomatic individuals with confirmed WT or hereditary amyloidosis, and asymptomatic carriers of variant TTR are eligible for enrollment. Data obtained during clinical evaluations are entered into the registry using a secure, interactive, web-based system.
Results: THAOS amyloidosis registry continues to grow steadily, with 2543 subjects enrolled from 17 countries. There are 295 WT subjects and 2243 subjects with variant TTR. Total of 81 mutations were recorded among subjects with variant with majority of them Val30Met (73.8%). Most WT subject are male (95.9%) while 50.7% male among the subjects with variant TTR. There are 2064 symptomatic patients (273 WT and 1791 hereditary amyloidosis) as well as 416 asymptomatic carriers of variant TTR. The median age of onset of symptoms for WT is 69.5 and for hereditary amyloidosis 39.5 (Val30Met 35.2, Non-Val30Met 52.5).
Conclusion: This analysis highlights the span and value of an international registry. THAOS registry data will help better characterize the diverse presentation and course of TTR amyloidosis and aid in improving diagnosis and treatment.

*IRB statement: All study sites obtained institutional and local review board approval prior to patient enrolment.

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Neuromuscular Disorders 1
Clinical spectrum and complications of Bell's palsy in a black South African population at the Dr George Mukhari Academic Hospital

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Objective: To assess the role of demographics, cardiometabolic risk and HIV on clinical patterns of Bell's palsy patients.
Methods: This was a retrospective analysis among black Bell's palsy patients admitted to a South African hospital between 2004 and 2012. Gender, age, clinical characteristics, HIV status, and CD4 counts were potential associate factors.
Results: Of 311 patients, 225 (72.3%), 173 (55.6%), 138 (44,4%), 106 (34.1%), 102 (32.8%), and 103 (33.1%) were HIV positive, females, males, age ≤25 years, 26–35 years, and ≥36 years, respectively. Older age was positively associated with hypertension and diabetes but negatively associated with hyperacusis and impaired taste. HIV was significantly more prevalent in impairment of taste (82.2% n = 83/101, OR = 2.2 95 %CI 1.2–4; P = 0.007) than in normal taste (67.7% n = 142/210) also with hyperacusis (95.8% n = 23/24, OR = 9.7 95% CI 1.3–7.28; P < 0.007) than normal hearing (70.4% n = 202/287). Among HIV positives, there was significant positive linear correlation between age (r = 0.263; P < 0.0001), females (yes = CD4 = 587.9 ± 308.7 cells/μL vs. males = CD4 = 498.9 ± 311.6 cells/μL; P = 0.033), hypertension (yes = CD4 = 665.7 ± 304.9 vs. no CD4 = 547.7 ± 308 cells/μL; P = 0.004), diabetes mellitus (yes = CD 4 = 727.2 ± 222.6 vs. no = CD4 = 535.2 ± 314 cells/μL; P = 0.021), and higher CD4 counts.
Conclusion: Comorbidities of Bell's palsy include HIV infection, hypertension and diabetes mellitus. Acute HIV and younger age might indicate severity in these black South Africans.

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Neuromuscular Disorders 1
Hypoglossal nerve palsy occurs from early infancy to late adulthood and is associated with a variety of etiologies

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Background: The medical literature contains many individual case reports and small series of hypoglossal nerve palsy (HNP). Apart from one large case series in 1996, there are no recent major retrospective series.
Objective: To report a retrospective case series of HNP from a multicampus academic institution describing initial symptoms and causes.
Patients/methods: With IRB approval, medical records from Mayo Clinic in Arizona, Florida and Minnesota were queried from 1984 to 2014, identifying 209 cases clinically diagnosed with HNP.
Results: Of 209 cases, 46.4% were female and 53.6% male. Median age was 58.0 years (range 0.0–90.0). The most common initial symptoms occurring in ≥99% were loss of tongue control, tongue swelling, tongue tightness, altered tongue sensation, tongue burning and odynophagia. Disease categories were malignant 29.8%, postoperative 28.4%, idiopathic 18.3%, inflammatory 5.8%, traumatic 4.8%, radiation 3.8%, vascular 2.9%, cyst-associated 2.4%, motor neuron disease 1.9% and congenital 1.9%. Some 49.8% were isolated HNP, 50.2% having involvement of other cranial nerves including optic 0.5%, oculomotor 3.3%, trochlear 1.0%, trigeminal 7.7%, abducens 7.7%, facial 10.0%, acoustic 3.3%, glossopharyngeal 5.3%, vagus 14.4% and spinal accessory 6.2%.
Conclusions: 1) The most common initial symptoms in HNP were loss of tongue control, tongue swelling, tongue tightness, altered tongue sensation, tongue burning and odynophagia. 2) The most frequent cause was malignancy followed by postoperative, idiopathic, inflammatory, traumatic, radiation, vascular, cyst-associated, motor neuron disease and congenital. 3) Diabetes mellitus was associated with HNP in 17.4% of cases but was seldom considered to be the sole potential etiologic factor.

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Neuromuscular Disorders 1
Development of a screening questionnaire for small-fiber polyneuropathy (SFPN)

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Background: SFPN is a polyneuropathy that predominantly affects small unmyelinated and thinly myelinated peripheral axons. Patients report varying combinations of sensory and autonomic symptoms, so clinical diagnosis is difficult. Recommended confirmatory objective tests, e.g., lower-leg skin biopsy or autonomic functioning testing (AFT), are expensive, invasive, and not widely available.
Objective: To develop a short, patient-completed, comprehensive symptom questionnaire to facilitate SFPN diagnosis and track treatment outcomes.
Patients and methods: This questionnaire was developed iteratively by concatenating validated questionnaires for pain and dysautonomic symptoms. Pre-field testing by patients undergoing evaluation for SFPN, followed by cognitive debriefing, eliminated redundant or unnecessary questions and captured new symptoms. 17 medical specialists then provided input. Descriptive analyses were performed and internal consistency was assessed.
Results: Among the 69 questionnaire-completers so far, 37 "gold-standard" subjects had SFPN confirmed by skin biopsy (31/37) and/or AFT (17/29). Their most prevalent sensory symptoms were "Tiredness" (95%), "Internal feeling of pains or aches" (89%), and "Tingling or pins and needles" (87%). Their most prevalent autonomic symptoms were "Feeling dizzy or faint while standing up" (73%), "Rapid heartbeat" (66%) and "Stomach full or bloated after meals" (61%). Cronbach's alpha revealed excellent internal reliability of 0.915, signaling diagnostic unity.
Conclusion: The final questionnaire may provide the first systematic, patient-based, quantification of SFPN symptoms. Predictive value is being assessed in a large, controlled study. A questionnaire that integrates all common SFPN symptoms holds promise for diagnosis and clinical research. We will work with multilingual collaborators to translate and validate it for global use.

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