MS / Neuroinflammatory Disease

P.016

Clinical course of relapsing remitting multiple sclerosis post-natalizumab

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Background: Natalizumab is an efficacious disease modifying therapy (DMT) for relapsing remitting multiple sclerosis (RRMS), however, duration of therapy is often limited by risk of progressive multifocal leukoencephalopathy (PML). We describe the clinical course of RRMS patients switched from natalizumab to another DMT in a Canadian MS clinic. **Methods:** We conducted a retrospective study of prospectively collected data from the Dalhousie Multiple Sclerosis Research Unit (DMSRU). We identified all RRMS patients treated with natalizumab for ≥3 months who discontinued therapy with serum JC virus antibody positive status and switched to another DMT. **Results:** There were 84 individuals who switched to another DMT following natalizumab with 57 (68%) switching to fingolimod. Survival without a relapse on fingolimod was 92% (95% confidence interval 80-97%) at 6 months, 90% (77-96%) at 12 months, 85% (71-93%) at 24 months, 74% (56-86%) at 36 months. Survival without disease progression on fingolimod was 90% (95% CI 78-96%) at 6 months, 86% (72-93%) at 12 months, 78% (63-88%) at 24 months, 78% (63-88%) at 36 months. **Conclusions:** Although alternative DMTs may be used post-natalizumab, fingolimod remains an effective therapy with a high proportion of patients remaining free of relapses or progression at 3 years.

P.017

Worldwide neurologist survey on management of autoimmune encephalitis

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Background: Diagnosis of autoimmune encephalitis (AE) is complicated by issues with sensitivity/specificity of antibody testing, non-specific MRI/EEG/CSF findings, and competing differential diagnoses. We explored practice differences in AE diagnosis and management. **Methods:** We utilized a worldwide electronic survey with practice-related demographic questions, and clinical questions about 2 cases: (1) a 20-year-old woman with a neuropsychiatric presentation strongly suspicious of AE, (2) a 40-year-old man with new temporal lobe seizures and cognitive impairment. Responses among different groups were compared using multi-variable logistic regression. **Results:** We received 1,333 responses from 94 countries; 12.0% identified as neuro-immunologists. **Case 1**: Those treating >5 AE cases/year were more likely to send antibodies in both serum and CSF (aOR vs 0/year: 3.29,95%CI 1.31-8.28,p=0.011), pursue empiric immunotherapy (aOR:2.42,1.33-4.40,p=0.004), and continue immunotherapy despite no response and negative antibodies at 2-weeks (aOR:1.65,1.02-2.69,p=0.043). **Case 2**: Neuro-immunologists were more likely to send antibodies in both serum and CSF (aOR:1.80,1.12-2.90,p=0.015). Those seeing >5 AE cases/year (aOR:1.86,1.22-2.86,p=0.004) were more likely to start immunotherapy without waiting for antibody results. **Conclusions:** Our findings highlight the heterogenous management of AE. Neuroimmunologists and those treating more AE cases generally take a more proactive approach to testing and immunotherapy than peers. Results emphasize the need for higher-quality treatment/outcome data and evidence-based guidelines.

P.019

Motor evoked potentials as a new biomarker in multiple sclerosis

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Background: Motor evoked potentials (MEP'S) measure myelin/axonal integrity of the central nervous system. MEP's reliability and correlation to conventional clinical measures in multiple sclerosis (MS) patients have yet to be demonstrated. Alemtuzumab is a high efficacy therapy used in patients with MS. Its longitudinal impact on electrophysiological measures has yet to be examined. **Methods:** This is a single center, observational study. 10 patients with MS who received their first cycle of alemtuzumab within less than 3 months were evaluated with both clinical and MEP's measures at baseline and every 6 months thereafter for 36 months. MEP's were repeated two weeks after every time point. We report our preliminary analyses. **Results:** Patient follow-up ranges from 6 to 36 months. The intraclass correlation coefficient (ICC) between two consecutive time points were good with values of 0.774 for the biceps and 0.867 for the tibialis anterior with p values less than 0.0005 for both. The correlation for the biceps MEP's to the 9 hole peg test (9HPT) was 0.51 with p less than 0.0005 and for the tibialis anterior MEP's to the 6 minute walk test (6MWT) was -0.411 with p=0.01. **Conclusions:** Our preliminary analyses demonstrate that MEP results are reproducible and correlate with clinical measures.

Neuro-oncology

P.020

Avelumab in newly diagnosed glioblastoma multiforme-the SEJ study

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Background: Glioblastoma Multiforme (GBM) has well documented systemic and local immunosuppressive mechanisms to escape immune surveillance and grow. GBM tumor cells as well as the microglia within it have a high incidence of PD-L1 surface

expression which makes it more susceptible to anti-PD-L1 antagonism and ADCC through avelumab therapy. **Methods:** This is a single center, phase 2, open label, add-on, single dose study of 156 weeks duration in patients receiving standard therapy for newly diagnosed GBM. In total 30 patients will be entered into the study within 3 weeks of finishing their last day of combined radiotherapy/temozolomide. The following are the results of the first interim analysis completed when the first eight patients completed 52 weeks or an end of study visit. **Results:** 24 patients have so far started therapy. There as been no unexpected treatment emergent adverse event (TEAE). Two patients transiently withheld therapy because of immune related TEAE's and none permanently. The objective response rate at week 52 for the first eight patients was 50% with 2 (25%) having a complete response and 1 (12.5%) a partial response. **Conclusions:** These preliminary results suggest that the addition of avelumab to standard therapy in patients with GBM is safe. Efficacy trends look promising.

Neurocritical Care

P.021

Esophageal cooling for hypoxic ischemic encephalopathy: a feasibility study

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Background: Targeted temperature management (TTM) is a recognized treatment to decrease mortality and improve neurological functionin hypoxic ischemic encephalopathy (HIE). An esophageal cooling device (ECD) has been studied in animal models but human data is limited. ECD appear to offer similar benefits to intravascular cooling catheters with potentially less risk to the patient. We studied whether the ECD could act as a substitute for intravascular cooling catheters. **Methods:** Eight ICU patients admitted following cardiac arrest who required TTM were enrolled prospectively. The primary outcome measures were timeliness of insertion, ease of insertion, user Likert ratings, time to achieve a target temperature of 36˚C and time target temperature was maintained within 0.5˚C of the 36˚C goal for 24 hours using an ECD. **Results:** Time to reach target temperature 0 min to 540 min. ECD appeared to be effective at maintaining a target temperature of 36˚C for most patients. In general, the catheter was easy to insert and use. **Conclusions:** For patients requiring TTM, use of an ECDadequately allowed for TTM goalsto be achieved and maintained. Overall user evaluationwas positive.

Neuromuscular Disease and EMG

P.022

Myasthenia gravis following dabrafenib and trametinib for metastatic melanoma

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Background: Inhibitors of BRAF and MEK, enzymes in the mitogen-activated protein kinase (MAPK) pathway, are now widely used in the treatment of metastatic melanoma. We report a case of acetylcholine receptor (AChR) antibody-positive myasthenia gravis developing after exposure to dabrafenib, a BRAF inhibitor, and trametinib, a MEK inhibitor. **Methods:** A 68-year-old man presented with dysarthria, dysphagia, cough, dyspnea, and fever. Examination revealed fatigable ptosis and proximal muscle weakness. He had started dabrafenib and trametinib for metastatic melanoma two weeks prior. He was diagnosed with myasthenia gravis and superimposed aspiration pneumonia. AChR antibodies were positive. Dabrafenib and trametinib were stopped. He improved rapidly with pyridostigmine alone, and remained free of myasthenic symptoms for the next two months. Another course of dabrafenib and trametinib was given, and seven weeks later, his myasthenic symptoms recurred. Pyridostigmine produced only partial improvement, and treatment with intravenous immunoglobulin and prednisone was initiated. **Results:** We are unaware of prior reports of an association between BRAF/MEK inhibitors and seropositive myasthenia gravis. The development of myasthenic symptoms twice after BRAF/MEK inhibitor exposure suggests that the association is more than coincidental. **Conclusions:** Myasthenia gravis may be a complication of treatment of melanoma with dabrafenib and trametinib. The mechanism by which this occurs is unknown.

P.023

Eculizumab shows consistent improvements across muscle groups in patients with AChR antibody-positive refractory myasthenia gravis

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Background: The physician-reported Quantitative Myasthenia Gravis (QMG) test was a key efficacy measure in REGAIN, a 26-week, phase 3, placebo-controlled study of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalized MG. Ocular and generalized weakness have shown variable responses to therapies including prednisone and intravenous immunoglobulin/plasma exchange. Using the patient-reported MG Activities of Daily Living (MG-ADL) scale during REGAIN, eculizumab showed a consistent trend toward rapid and sustained improvement across bulbar, respiratory, limb and ocular domains. We analyzed the effect of eculizumab on bulbar, respiratory, gross motor and ocular domains during REGAIN, using the QMG test. **Methods:** QMG domain score changes to REGAIN week 26 were determined for patients with abnormal baseline scores. Repeated-measures analyses were performed for bulbar (swallowing/speech), respiratory (forced vital capacity),