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October 07, 2022 | Webinar

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38 YEARS OF EXCELLENCE IN MEDICAL PUBLISHING

12th International Conference on
Central Nervous System

October 07, 2022 | Webinar

Received date: 01 October 2022 | Accepted date: 04 October 2022 | Published date: 20 October 2022

A case report: Optic neuritis as a primary manifestation of Multiple sclerosis in a patient treated with TNF-α inhibitors

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Introduction: Multiple sclerosis (MS) often manifests with a degree of visual dysfunction which can significantly impair the quality of life. Optic Neuritis (ON) is a common demyelinating disorder and may be a presenting feature of MS in up to 20% of patients (1). Tumour Necrosis Factor alpha (TNF-α) inhibitors are used for suppression of inflammatory processes in autoimmune diseases and arthritides. Despite a relatively good safety profile, there have been several reports of newly-onset central nervous system demyelinating manifestations, suggesting a causal role of TNF-α inhibitors (2, 3). We present a case of ON as a primary presentation of MS in a patient undergoing treatment with TNF-α blockers.

Case Report: A 21-year-old female presented with a 4-day blurring of vision in the left eye, accompanied by painful ocular motility. For the past 6 years she had been receiving treatment with monthly injections of etanercept due to juvenile idiopathic arthritis. She had a positive family history of MS. Ophthalmic examination revealed Best Corrected Visual Acuity (BCVA) of 0, 3 Snellen, and positive Relative Afferent Pupillary Defect (RAPD) and decreased colour perception (Ishihara test 9/21) in the left eye. Optic disc was swollen with irregular obscuration of borders (Figure 1) and Optic Coherence Tomography (OCT) showed increased thickness of peripapillary Retinal Nerve Fibre Layers (RNFL) (Figure 2a). Standard automated perimetry (SAP) showed significant diffusely decreased sensitivity, with nearly complete inferior altitudinal defect (Figure 3a). Right eye examination was unremarkable. She underwent neurologic examination without apparent anomalies. Head MRI revealed several typical demyelinating lesions (Figure 4). Lumbar puncture was performed, and the patient received intravenous pulse corticosteroid therapy (3 days of 1000 mg methylprednisolone daily). After three pulses, BCVA of the left eye increased to 1, 0 Snellen and colour perception improved (Ishihara test 21/21). Ocular motility pain and optic disc swelling were somewhat diminished. Upon discharge she commenced a corticosteroid tapering scheme with initial dose of 64 mg. At the last follow up, 2 weeks after discharge, there were no further symptoms reported, BVCA remained 1,0 Snellen and ocular motility was painless in the left eye. Ophthalmic examination showed some residual optic disc swelling. OCT showed improvement in thickness of RNFL layers (Figure 2b) and SAP had few non-specific localised spots of decreased sensitivity (Figure 3b).

Conclusion: While TNF-α inhibiting medication represents a crucial breakthrough in the treatment of arthritis, its effects on demyelination processes remain incompletely understood. Further research is needed to achieve better insight into the relationship with MS. Any patients on TNF-α medication should be closely monitored for any newly developed neurologic signs or symptoms.

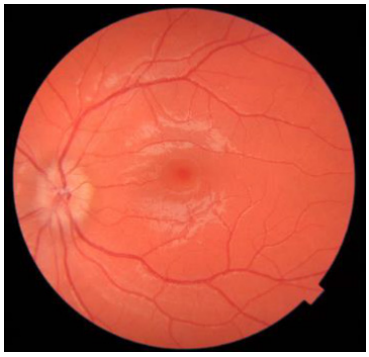

Figure 1: Optic nerve photograph of the left eye with swollen optic disc and irregular borders.

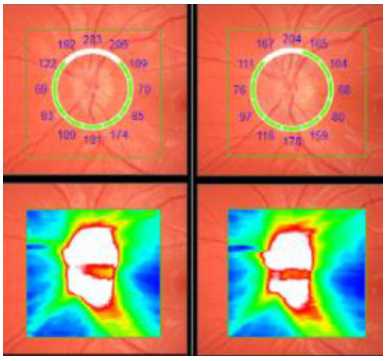

Figure 2: Optic coherence tomography showing thickened retinal nerve fibre layers of the left optic nerve at presentation (2a) and after treatment (2b).

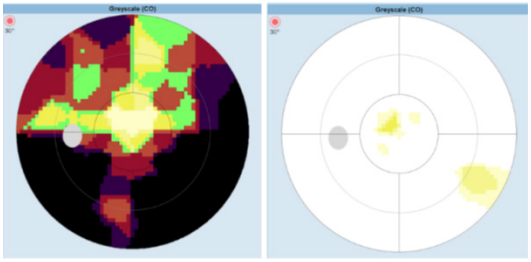

Figure 3: Standard automated perimetry at presentation (3a) with diffuse decrease in sensitivity and altitudinal visual field defect, MD 19,7 dB, slV 7,6 dB; with improvement after treatment, MD 0,8 dB2,4 dB, slV (3b).

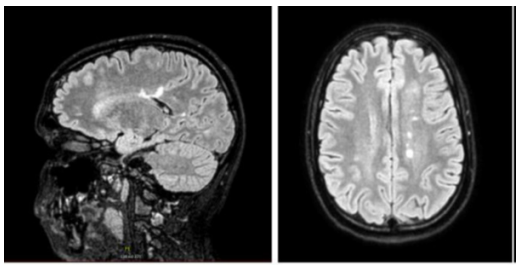

Figure 4: Sagital FLAIR sequence image demonstrating typical ovoid hyper intensive periventricular lesions (called Dawson fingers). Axial FLAIR sequence image with several periventricular white matter hyper intensive lesions.

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1. Frohman EM, Frohman TC, Zee DS, McColl R, Galetta S. The neuro-ophthalmology of multiple sclerosis. Lancet Neurol. 2005 Feb;4(2):111–21.
2. Kemanetzoglou E, Andreadou E. CNS Demyelination with TNF-α Blockers. Curr Neurol Neurosci Rep. 2017 Apr;17(4):36.
3. Mohan N, Edwards ET, Cupps TR, Oliverio PJ, Sandberg G, Crayton H, et al. Demyelination occurring during anti-tumor necrosis factor alpha therapy for inflammatory arthritides. Arthritis Rheum. 2001 Dec;44(12):2862–9.

Biography

Nina Špegel is currently working as a trainee doctor in an Ophthalmologist's office. In her work she often comes across patients whose pathology exceeds purely ocular manifestations, therefore she finds a multidisciplinary approach essential to provide a high standard of patient care.

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Central Nervous System

October 07, 2022 | Webinar

Accepted Abstracts

38 YEARS OF EXCELLENCE IN MEDICAL PUBLISHING

12th International Conference on
Central Nervous System

October 07, 2022 | Webinar

Received date: 26 July 2022 | Accepted date: 29 July 2022 | Published date: 20 October 2022

Theoretical discrimination index of postural instability in Amyotrophic Lateral Sclerosis

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Objective: To assess the usefulness of a theoretical postural instability discrimination index (PIth) in amyotrophic lateral sclerosis (ALS).

Methods: Prospective regression analyzes were performed to identify the biomechanical determinants of postural instability unrelated to lower limb motor deficits from gait initiation factors. PIth was constructed using a logit function of biomechanical determinants. Discriminatory performance and performance differences were tested.

Results: Backward displacement of the pression center (APAamplitude) and active vertical braking of the mass center (Braking-index) were the biomechanical determinants of postural instability. PIth = - 0.13 x APAamplitude – 0.12 x Braking-index + 5.67, ($P < 0.0001$, RSquare = 0.6119). OR(APAamplitude) and OR(Braking-index) were 0.878 and 0.887, respectively, i.e., for a decrease of 10 mm in APAamplitude or 10% in Braking-index, the postural instability risk was 11.391 or 11.274 times higher, respectively.

PIth had the highest discriminatory performance (AUC 0.953) with a decision threshold value ≥ 0.587, a sensitivity of 90.91%, and a specificity of 83.87%, significantly increasing the sensitivity by 11.11%.

Conclusion: PIth, as objective clinical integrator of gait initiation biomechanical processes significantly involved in dynamic postural control, was a reliable and performing discrimination index of postural instability with a significant increased sensitivity, and may be useful for a personalized approach to postural instability in ALS.

Recent Publications

1. Alexandre Vallée, Yves Lecarpentier, and Jean-Noël Vallée (2022). WNT/β-catenin pathway and circadian rhythms in obsessive-compulsive disorder. Neural Regen Res. 2022 Oct;17(10):2126-2130
2. Alexandre Vallée, Yves Lecarpentier, and Jean-Noël Vallée (2021) Cannabidiol and the Canonical WNT/β-Catenin Pathway in Glaucoma. Int. J. Mol. Sci. 2021, 22, 3798
3. Alexandre Vallée, Jean-Noël Vallée, Yves Lecarpentier (2021) Parkinson's Disease: Potential Actions of Lithium by Targeting the WNT/β-Catenin Pathway, Oxidative Stress, Inflammation and Glutamatergic Pathway. Cells. 2021 Jan 25;10(2):230

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12th International Conference on

Central Nervous System

October 07, 2022 | Webinar

Received date: 30 May 2022 | Accepted date: 02 June 2022 | Published date: 20 October 2022

Communication skills training pilot programme after Traumatic Brain Injury: Short and medium term benefits

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Objective: The study aimed to evaluate whether a pilot communication rehabilitation programme improves different communicative modalities in people who have sustained a moderate to severe TBI immediately following the training and at 3 months follow up.

Methods: We have recruited 12 participants who had moderate-to-severe TBI. Subjects were randomly divided into two groups, EG and CG. We have assessed the groups before and after treatment and we have performed a follow-up three months later, through of the ABaCo. The EG followed a very structured programme. In the CG, a programme to stimulate communication through free conversation was carried out. Each programme consisted of 24 group sessions, of 1h30 min, twice a week, for 12 weeks.

Results: Improvements were observed in both groups, although more evident in the EG. Both groups had better results in extralinguistic production. In the EG, there was still an improvement in the paralinguistic production and extralinguistic comprehension, after ending the training. These improvements persisted 3 months after ending the programme.

Conclusion: The results demonstrated the effectiveness of the intervention of a structured pragmatic rehabilitation programme. However, the existence of a communication group based solely on conversation can also have positive results and should be implemented whenever a more specific intervention is not possible. In future research, it will be important to increase the sample size and involve caregivers in person and regularly in the EG programme.

Recent Publications

1. Agrela, Santos & Sandra Guerreiro (2021): Communication skills training pilot programme after traumatic brain injury: short and medium-term benefits, Brain Injury.
2. Agrela N, Santos ME, Guerreiro S.Transcultural translation and adaptation of the Assessment Battery for Communication (ABaCo) for the Portuguese population. CEFAC Speech Lang Hear Sci Educ J. 2020;22(3):e15319.
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12th International Conference on
Central Nervous System

October 07, 2022 | Webinar

Received Date: 15 September 2022 | Accepted Date: 20 September 2022 | Published date: 20 October 2022

Jahi McMath: A new state of disorder of consciousness

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In this paper, I reviewed the case of Jahi McMath who was diagnosed as being in brain death (BD). Nonetheless, ancillary tests, performed 9 months after initial brain insult, showed conservation of intracranial structures, EEG activity, and autonomic reactivity to "Mother Talks" stimulus. She was clinically in a state of unarousable and unresponsiveness, without evidence of awareness of self or environment, but full absence of brainstem reflexes, and partial responsiveness rejected the possibility of being in coma. Jahi was not a UWS, because she was not in a wakefulness state, and showed partial responsiveness. LIS patients are wakeful and aware, and although these cases are quadriplegic, they fully or partially preserve brainstem reflexes, vertical eye movements, and/or blinking, and respire by their own, rejecting the possibility of classifying her as a LIS patient. She was not a MCS because she did not preserve arousal, and only partially preserved awareness. The CRS-R resulted in a very low score, not corresponding with MCS patients. MCS patients fully or partially preserve brainstem reflexes, and usually breathe by their own. MCS has been always described as a transitional state between coma, UWS, but MCS has never been reported in a patient who has all clinical BD findings. This case doesn't contradict the concept of BD, but brings again to discussion the needs of using ancillary tests in BD. I concluded that Jahi represented a new state of disorder of consciousness, non-previously described, that I have termed: "responsive unawake syndrome" (RUS).

Recent Publications

1. Machado-Curbelo C, Gonzalez-Quevedo A. Hypoxemia and Cytokine Storm in COVID-19: Clinical Implications. MEDICC Review July 2021, Vol 23, No 3;
2. Machado C, Brock JB, Machado Y, Chinchilla M. An early prevention of hypoxemia in COVID-19 patients complaining obstructive sleep apnea. Sleep Medicine 2021; 85(2);
3. Machado C. Reader Response: Early Postmortem Brain MRI Findings in COVID-19 non-survivors. Neurology 2021;97(5):253

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12th International Conference on
Central Nervous System

October 07, 2022 | Webinar

Received date: 22 July 2022 | Accepted date: 26 July 2022 | Published date: 20 October 2022

Placental transfer of essential micronutrients and toxic metals in occupationally exposed pregnant women- Implications in the pathogenesis of Autism spectrum disorders

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Background: Autism Spectrum Disorders (ASD) is a neurodevelopmental abnormality. In spite of genetic mappings and investigation of environmental toxicants, aetiogenesis of this disorder remains a medical challenge. This work investigated placental transfer of some trace metals (Cu, Zn, Ca, Mg, Se, Cd, Pb) in occupationally vulnerable pregnant mothers as possible basis of ASD in children.

Method: 105 third trimester pregnant women comprising 50 occupationally exposed (cases) (27.68±5.57 years) and 55 non-occupationally exposed age-matched (28.84±5.37 years) (controls) were recruited for this study. Blood (including cord blood) was collected from all participants. Trace metal levels were determined in the blood samples using Induction-Coupled Plasma-Mass Spectroscopy (ICP-MS); anthropometric and sociodemographic data of the women including developmental milestone indices of the baby at infancy were also recorded.

Results: Levels of trace elements were 328.02±109.99mg/L, 370.82±192.97umol/L, 8.61±0.89mg/dl, 1.52±0.26mg/dl and 10.17±1.22mg/L; 348.27±150.61mg/L, 416.80±276.73umol/L, 8.61±0.86mg/dl, 1.46±0.35mg/dl and 8.96±1.15 mg/L for Cu, Zn, Ca, Mg and Se in cases and controls respectively. The differences were not significant. Less than 10% of participants samples (maternal and cord blood) had detectable toxic metal levels. However, cord blood trace metals concentrations were 125.07±24.66mg/l, 525.38±45.86umol/L, 8.44±0.15mg/dl, 1.51±0.31mg/dl and 7.02±0.72mg/dl in fetuses of cases and 91.05±13.27mg/l, 591.22±44.62umol/l, 1.63±0.15mg/dl and 8.19±0.78mg/L in fetuses of control for Cu, Zn, Ca, Mg and Se respectively. Only cord blood Mg level was significantly different (p=0.013). Baby weight and head circumferences also correlated significantly with cord Zn and Cu levels (r=0.293, p=0.039), (r=0.478, p=0.010) respectively.

Discussion: Reduction in Mg and Se levels may have depleted the antioxidant pool overwhelming the protective roles of glutathione and zinc as antioxidants in the fetuses thereby precipitating abnormal genetic configurations in the developing baby. Our hypothesis is that given the role of Se, Cu and Mg in neurodevelopment, imbalance of these metals from in-utero may be the aetiological basis of ASD in children.

Recent Publications

1. Omotosho, IO Akinade, AO;, Lagunju, IA. (2017). Calcium and Magnesium levels are down regulated in Nigerian children with Autism Spectrum Disorder and Cerebral Palsy: Neuroscience and Medicine Vol 9 (3); 159-170
2. Akinade, AO, Omotosho, IO, Lagunju, IA. Yakubu, MA (2019) Environmental Exposure to Lead, Vanadium, Copper and Selenium: Possible Implications in the Development of Autism Spectrum Disorders Neuroscience & Medicine,10, 247-258
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