2772 NEW DIAGNOSIS OF MITOCHONDRIAL ENCEPHALOPATHY, LACTIC ACIDOSIS, AND STROKE-LIKE EPISODES (MELAS) PRESENTING AS BILATERAL CEREBRAL INFARCTS

[1]Oshi Swarup*, [1,2]Nawaf Yassi, [3,4]Timothy Fazio, [3]Sarah Donoghue, [1]Stephen Davis. *[1]Department of Neurology, Melbourne Brain Centre, Royal Melbourne Hospital and University of Melbourne, Melbourne, VIC, Australia*; *[2]Population Health and Immunity Division, The Walter and Eliza Hall Institute of Medical Research, Melbourne, VIC, Australia*; *[3]Metabolic Diseases Unit, Royal Melbourne Hospital, Melbourne, VIC, Australia*; *[4]Melbourne Medical School, University of Melbourne, Melbourne, VIC, Australia*

10.1136/bmjno-2023-ANZAN.138

Background Mitochondrial disorders can manifest in stroke-like episodes which can pose several diagnostic and management challenges in the acute setting.

Presentation We present the case of a 45-year-old female, presenting with bilateral cerebral infarcts on a background of cerebral atrophy, cognitive decline, ataxia, sensorineural hearing loss, peripheral neuropathy, Type 1 Diabetes mellitus, and androgen insensitivity syndrome with investigations revealing a new diagnosis of Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like episodes (MELAS).

Management and Outcomes Initial diagnostic investigations revealed an elevated serum and cerebrospinal fluid lactate, and MRI Brain revealed bilateral cerebral infarcts. Genetic testing on blood confirmed the presence of the m.3243A>G pathogenic variant in the mitochondrial gene *MT-TL1*, one of the common genetic mutations causing MELAS in the caucasian population. The heteroplasmy level on the sample was 24.6%. Further cascade testing identified several other affected family members. Ultimately, the patient was managed with oral arginine and subsequently oral taurine for secondary stroke prevention.

Discussion This case demonstrates the importance of recognising mitochondrial disorders in atypical stroke presentations as the acute and long-term treatments can vary from standard stroke care. While treatment with arginine therapy acutely is established in management of stroke-like presentations in MELAS, taurine therapy has also demonstrated potential reduction in stroke-like events in this patient group.[1 2] Making an accurate diagnosis is important in guiding long term management, family counselling and identifying relatives at risk who would benefit from early arginine treatment when presenting with stroke-like episodes, and screening for associated co-morbidities.

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2773 NOVEL *BAG3* VARIANT IDENTIFIED IN A CASE OF ADULT-ONSET MYOFIBRILLAR MYOPATHY

[1,2]Tram BT Nguyen*, [2,3]Richard Lin, [3,4]Suzanna EL Temple, [1]Henry LT Vo, [1]Daniel S Green, [5,6]Anthony Cheong, [7]Roger Pamphlett, [1]Zeljka Calic. *[1]Department of Neurology, Liverpool Hospital, Liverpool, NSW, Australia*; *[2]South West Sydney Clinical School, UNSW Sydney, Sydney, NSW, Australia*; *[3]Department of Clinical Genetics, Liverpool Hospital, Sydney, NSW, Australia*; *[4]School of Paediatrics, UNSW Sydney, Sydney, NSW, Australia*; *[5]Molecular Medicine Laboratory, Concord Repatriation General Hospital, Sydney, NSW, Australia*; *[6]Sydney Medical School, University of Sydney, Sydney, NSW, Australia*; *[7]Department of Neuropathology, Brain and Mind Centre, Royal Prince Alfred Hospital, Sydney, NSW, Australia*

10.1136/bmjno-2023-ANZAN.139

Objectives Myofibrillary myopathies (MFM) are a heterogenous group of disorders characterised by myofibrillar dissolution and accumulation of protein degradation products in myofibres. *BCL2-associated anthanogene 3* (*BAG3*)-related MFM has been reported to present with sensorimotor neuropathy and cardiomyopathy. We report a case of a 54-year-old man with a progressive sensorimotor axonal neuropathy with respiratory involvement who was found to have a novel *BAG3* variant.

Case A 54-year-old man presented with a six-month history of increasing dyspnoea with severe restrictive ventilatory dysfunction evident on pulmonary function testing. He has a five-year history of progressive sensorimotor disturbance in his limbs with muscle cramps and gait impairment leaving him wheelchair-bound. Examination revealed marked wasting and florid fasciculations in the upper and lower limbs, distal greater than proximal weakness, absent reflexes and a stocking-and-glove distribution sensory disturbance. Electrodiagnostic studies confirmed a severe length-dependent sensorimotor axonal neuropathy with active and chronic denervation on electromyography. Singleton whole exome sequencing identified a heterozygous missense variant of unknown significance in *BAG3* [NM_004281.3:c.625C>G, p.(Pro209Ala)]. Other variants in *BAG3* at the same amino acid residue [p.(Pro209Leu) and p.(Pro209Gln)] have been reported to be associated with *BAG3*-related MFM. Subsequent muscle biopsy demonstrated chronic denervation and reinnervation of myofibres with pseudodystrophic changes, suggestive of an underlying myofibrillar myopathy. He was managed supportively with nocturnal bilevel positive airway pressure and discharged into supported accommodation.

Conclusion This is a case of adult-onset myofibrillary myopathy suspected to be due to a novel missense *BAG3* variant located in a previously reported *BAG3* mutation hotspot (Proline 209).

2774 PLANNED DOSE REDUCTION OF OCRELIZUMAB IN RELAPSING-REMITTING MULTIPLE SCLEROSIS: A SINGLE CENTRE OBSERVATIONAL STUDY

[1]Trung Tran*, [2]Mike Boggild. *[1]James Cook University, Townsville, QLD, Australia*; *[2]Department of Neurology, Townsville University Hospital, Townsville, QLD, Australia*

10.1136/bmjno-2023-ANZAN.140

Background Ocrelizumab, a humanised anti-CD20 monoclonal, is a highly effective treatment for relapsing-remitting multiple sclerosis (RRMS). Long-term safety of B-cell depletion in RRMS is uncertain and there is no data on dose reduction of ocrelizumab as a risk mitigation strategy. Experience with rituximab suggests dose reduction paradigms may maintain efficacy whilst reducing side effects.
Objectives To evaluate effectiveness and safety of reducing ocrelizumab dose from 600 to 300mg every 6 months in patients with RRMS.
Methods Data was collected through the Townsville neurology service. Following standard randomised controlled trial regimen of 600mg every 6 months for 2 years, patients consented to dose reduction to 300mg every 6 months. Patients were included if they were diagnosed with RRMS, and received at least one reduced dose of ocrelizumab. Relapse, disability progression, new magnetic resonance imaging (MRI) lesions, CD19+ cell count, and immunoglobulin concentrations were analysed.
Results 29 patients were included, a total of 150 full and 86 reduced doses, mean follow-up on reduced dose was 17 (1–28) months. We observed no relapse or new MRI activity in the cohort receiving the reduced dose. No new safety concerns arose. Data regarding disability, CD19+ cell counts and immunoglobulin concentrations will be reported.
Conclusions In this single-centre observational study, dose reduction of ocrelizumab from 600 to 300mg every 6 months after 2 years appeared to maintain efficacy in terms of new inflammatory disease activity. A randomised trial may be warranted to confirm this and explore the impact of dose reduction on long-term safety.

2775 HIDING IN PLAIN SIGHT, AN ASSOCIATION TO REMEMBER: SEVERE HYPOVITAMINOSIS A, SKULL HYPEROSTOSIS AND COMPRESSIVE OPTIC NEUROPATHY

[1,2]Michael Ginevra*, [1]Nicholas Caldwell, [1,3]Rohit Sharma, [1]Lakshini Gunasekera, [1]Abhishek Malhotra. *[1]Department of Neurosciences, Barwon Health, Geelong, Victoria, Australia; [2]Department of Neurology, Austin Health, Heidelberg, VIC, Australia; [3]Department of Neurology, Alfred Health, Melbourne, VIC, Australia*

10.1136/bmjno-2023-ANZAN.141

Objectives We present a case of severe painless progressive bilateral visual loss in a young male with severe vitamin A deficiency associated with skull hyperostosis and compressive optic neuropathy. This case highlights and adds to the literature of this rarely described triad with severe hypovitaminosis A.
Method Case Report
Results A 20-year-gentleman presented with six weeks of severe progressive painless visual loss resulting in a visual acuity limited to perception of hand movements. This is on a background of obesity and a restrictive diet. There were no antecedent infective symptoms, vaccination or past neurological or visual symptoms. The MRI showed hyperostosis of the skull especially affecting the skull vault with features suggestive of bilateral compressive optic neuropathy He underwent anterior clinoidectomy for optic nerve decompression along with a three day course of intravenous methylprednisolone Lactate, blood sugar, vasculitis screen and autoimmune markers were unremarkable. The CSF analysis was non-inflammatory. Investigations. revealed severe vitamin A and vitamin B12 deficiency. Visual acuity improved to 6/60 at time of discharge following surgery and vitamin replacement therapy.
Conclusion Hypovitaminosis A can be associated with skull hyperostosis and compressive optic neuropathy. Previous literature described a similar triad mainly in patients with autism spectrum disorder and restrictive eating patterns. They were also associated with other fat soluble vitamin deficiencies particularly vitamin B12. Ophthalmic findings of xerophthalmia and nyctalopia are often seen but may not be present. Prompt vitamin replacement therapy and decompressive surgery needs to considered in these cases to preserve and improve vision.

2777 HYPERTROPHIC OLIVARY DEGENERATION SECONDARY TO LONG-STANDING BRAINSTEM AND CEREBELLAR CAVERNOMATA

[1]Liam Mulcahy, [2,3,4,5]Neha Irani, [2,6,7]Kevin O'Connor, [2,8]Dev Nathani, [2,9,10]Shivlal David. *[1]Stroke, Ramsay Health Care, Perth, WA, Australia; [2]Neurology, Joondalup Health Campus, Perth, WA, Australia; [3]Neurology, Fiona Stanley Hospital, Perth, WA, Australia; [4]Ophthalmology, Sir Charles Gardiner Hospital, Perth, WA, Australia; [5]Ophthalmology, Royal Perth Hospital, Perth, WA, Australia; [6]Neurology, Royal Perth Hospital, Perth, WA, Australia; [7]Immunology, Royal Perth Hospital, Perth, WA, Australia; [8]Neurology, Perron Institute for Neurological and Translational Science, Perth, WA, Australia; [9]Geriatric Medicine, Joondalup Health Campus, Perth, WA, Australia; [10]Geriatric Medicine, PRACWA, Perth, WA, Australia*

10.1136/bmjno-2023-ANZAN.142

Introduction Hypertrophic olivary degeneration (HOD) is a rare complication of brainstem cavernoma.
Case Report We present a case of a 66-year-old man with 12-month history of progressive ataxia, dysarthria, ophthalmoplegia and palatal tremor. Remote medical history is notable for two previous strokes, at ages of 4 and 24 years, presumed to be haemorrhagic, although medical records from four decades prior were not available for confirmation.

Examination was notable for severe dysarthria, right gaze palsy along with partial internuclear ophthalmoplegia (partial one-and-a-half syndrome), right fascicular abducens nerve palsy, gaze evoked jerk nystagmus, skew deviation, rhythmic palatal tremor, mild left facial nerve palsy, left upper and lower limb weakness and hypertonia, moderately severe bilateral upper and lower limb ataxia.

CT and MRI brain demonstrated multiple supra and infratentorial cavernomata, prominently in pons and right cerebellum. There was subacute haemorrhage into a right thalamic cavernoma and T2-hyperintensity in both olivary nuclei, characteristic of HOD. Based on available neuroimaging from 12 years prior, the right cerebellar cavernoma and HOD were new findings along with enlargement of the pontine cavernoma. FDG-PET scan demonstrated hypometabolism involving bilateral, right more than left, cerebellar hemispheres and the pons.
Discussion Brainstem cavernoma as the aetiology of HOD is extremely rare. Although this patient did not present with symptomatic brainstem haemorrhage, it is likely that he had subclinical haemorrhage leading to Wallerian degeneration and subsequent development of HOD. This case sheds light on the natural history of brainstem cavernoma and highlights the rare potential complication of HOD.