consult neurology service. Decision for referral may be influenced by uncertainty of diagnosis and referrer's clinical confidence in identifying risks of secondary causes. We examined the effect of an online guideline for adult headache on referrals to neurology service, and analyse the quality of the referrals and outcome of their clinical assessment.

Methods We examined the referrals in selected months within 2 years before and 2 years after online publication of a headache guideline developed by our neurology department. Referrals for headaches being the primary complaint were analysed. The primary outcome was the proportion of neurology referrals for headache as the primary complaint pre- versus post guideline.

Results Nine hundred neurology referrals before and 801 neurology referrals after the publication of online headache guideline were included. There was a significant reduction in proportion of neurology referrals for headaches (OR = 0.73 (0.55 – 0.96), $p = 0.026$). The proportion of headache referrals requiring face-to-face assessment in clinic was also reduced from 69% before and 53% after publication of the headache guideline ($p=0.014$). There are similar proportions of patient referred without adequate trial of preventative medication prior (33.8% vs. 27.7%), and over used analgesics (21.9% vs. 25.0%).

Conclusions The headache guideline demonstrated effectiveness in reducing demand for assessment of headaches in neurology clinic. Headache management prior to referral is an ongoing area of concern.

055 AN UNUSUAL PRESENTATION OF SOD1-ALS: A CASE REPORT

¹Allycia MacDonald*, ²Jason Dyke, ³Simon Khangure, ¹Andrew Kelly. ¹Department of Neurology, Fiona Stanley Hospital, Murdoch, WA, Australia; ²Anatomical Pathology, PathWest, Nedlands, WA, Australia; ³Department of Radiology, Fiona Stanley Hospital, Murdoch, WA, Australia

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Introduction Approximately 10% of amyotrophic lateral sclerosis (ALS) cases are inherited, of which 20% are due to mutations in the superoxide dismutase-1 gene (SOD1). MRI abnormalities are not uncommon in ALS, and there have been previous case reports of peripheral nerve enhancement in patients with SOD1 mutations, typically attributed to rapid neuronal degeneration.

Case A 31-year-old previously well Malaysian woman presented with a 3 month history of progressive lower limb weakness, initially involving the right lower limb but progressing to involve the left, requiring the use of a walking aid. Initial examination demonstrated asymmetric upper and lower motor neuron signs in bilateral upper and lower limbs. EMG findings were of a severe pure motor axonal process. CSF examination revealed elevated protein without significant elevation of white cells. MRI brain and spine demonstrated smooth cauda-equina ventral nerve root thickening and enhancement. Treatment with intravenous immunoglobulin and high dose corticosteroid was commenced for a presumed inflammatory process, with no clinical improvement. A cauda-equina nerve root biopsy was performed, demonstrating features consistent with an immune-mediated demyelinating neuropathy. The patient

continued to deteriorate, developing flaccid upper limb weakness and facial involvement. Plasma exchange, azathioprine, cyclophosphamide, and rituximab were sequentially administered over the following two months without altering the rate of disease progression. Genetic testing returned a positive SOD1 heterozygous gene mutation, confirming the diagnosis of ALS.

Conclusions We present a case of SOD1-ALS with atypical features on imaging and histopathology suggesting an underlying demyelinating process, expanding the known clinical spectrum of this mutation.

056 EFFICACY AND SAFETY OF THE BRUTON'S TYROSINE KINASE INHIBITOR EVOBRUTINIB (M2951) IN PATIENTS WITH RELAPSING MULTIPLE SCLEROSIS OVER 48 WEEKS: A RANDOMIZED, PLACEBO-CONTROLLED, PHASE 2 STUDY

^{1,2}Xavier Montalban, ^{3,4}Douglas L Arnold, ^{5,6}Martin S Weber, ⁷Ivan Staikov, ⁸Karolina Piasecka-Strczynska, ⁹Alan Gillett, ¹⁰Emily C Martin, ¹⁰Sana Syed*, ¹⁰Fernando Dangond, ¹¹Jerry S Wolinsky. ¹Vall d'Hebron University Hospital, Barcelona, Spain; ²University of Toronto, Toronto, Canada; ³Montreal Neurological Institute and Hospital, Montreal, Canada; ⁴NeuroRx Research, Montreal, Canada; ⁵Institute of Neuropathology, Universitätsmedizin Göttingen, Göttingen, Germany; ⁶Department of Neurology, Universitätsmedizin Göttingen, Göttingen, Germany; ⁷Department of Neurology, Acibadem City Clinic Tokuda Hospital, Sofia, Bulgaria; ⁸Outpatient Neurology Clinic, Hanka Hertmanowska MS Care Center, Plewiska, Poland; ⁹EMD Serono, Mississauga, ONTARIO, Canada; ¹⁰Global Clinical Development Center, EMD Serono, Billerica, MA, USA; ¹¹McGovern Medical School, University of Texas Health Science Center at Houston (UTHealth), Houston, TX, USA

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Introduction Evobrutinib (M2951) is a highly specific oral inhibitor of Bruton's tyrosine kinase, a key regulator of B cell and macrophage functions implicated in MS.

Methods In this double-blind, phase 2 study (NCT02975349), adult patients (≤ 65 years) with relapsing MS (RMS) were randomized to evobrutinib 25 mgQD, 75 mgQD, 75 mgBID, placebo, or open-label dimethyl fumarate (240 mgBID; reference arm) for 48 weeks; placebo-treated patients switched to evobrutinib 25 mgQD after 24 weeks. The primary endpoint was the total number of T1 gadolinium-enhancing (T1Gd+) lesions at Weeks 12, 16, 20, and 24. Secondary endpoints included annualized relapse rate (ARR), MRI measures at Weeks 24 and 48, and safety.

Results Among 261 patients, the sum of T1Gd+ lesions over Weeks 12–24 was reduced with evobrutinib 75 mgQD ($p=0.002$) and 75 mgBID ($p=0.03$); a dose response was observed ($p=0.001$). There was no evidence of change in effect on T1Gd+ lesions (mean $\pm$ SD; Wilcoxon signed-rank test) between Weeks 24 and 48 with evobrutinib 75 mgQD (0.28 ± 0.91 to 0.85 ± 2.87 ; $p=0.57$) or 75 mgBID (0.24 ± 0.88 to 0.49 ± 1.22 ; $p=0.23$). ARR (unadjusted [95%CI]) was 0.25 (0.12–0.44) for evobrutinib 75 mgQD and 0.11 (0.04–0.25) for 75 mgBID over 48 weeks, and 0.37 (0.17–0.70) for placebo over 24 weeks. Evobrutinib appeared well-tolerated. Shifts to Grade 3–4 ALT and AST elevations from normal (grade 0) occurred in 8 (5.4%) and 6 (3.9%) evobrutinib-treated patients respectively, driven by events with onset within the first 24 weeks.

Conclusions Evobrutinib is the first BTK inhibitor to demonstrate disease activity reduction in RMS. The observed benefit-risk profile supports further clinical development.

057 A RARE PRESENTATION OF A RARE DISEASE: ADULT ONSET KRABBE'S DISEASE PRESENTING WITH PROGRESSIVE HYPERTROPHIC POLYRADICULONEUROPATHY

Allycia MacDonald*, Phillipa Lamont, Wai Leong. *Department of Neurology, Royal Perth Hospital, Perth, WA, Australia*

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Introduction Globoid Cell Leukodystrophy (Krabbe's disease) is a rare autosomal recessive condition caused by defects in the lysosomal enzyme galactosylceramidase. The disease typically occurs in infants and is rapidly progressive. Fewer than 5% of cases develop symptoms in adulthood, the majority of which present with spastic paraparesis.

Case A 40-year-old Italian man presented with a 20 year history of gradually progressive asymmetrical hand paraesthesias and weakness. EMG demonstrated demyelinating features and absent sensory responses. CSF examination revealed elevated protein with no cells and negative oligoclonal bands. Treatment with intravenous immunoglobulin (IVIg) was commenced and continued for 2 years for presumed CIDP without clinical response. Upper limb wasting and weakness progressed over the following 10 years with associated loss of reflexes, prompting consideration of an underlying genetic neuropathy. DNA testing for common CMT mutations was negative. MRI cervical spine and brachial plexus demonstrated diffuse bilateral non-enhancing enlargement of cervical nerve roots. IVIg was recommenced over the next 10 years with continued clinical deterioration to the point of bilateral flail arms with relatively preserved lower limb motor function, in addition to bulbar and respiratory dysfunction by age 64. MRI brain demonstrated thickening of a number of cranial nerves without contrast enhancement, and extensive T2-hyperintensity of periventricular white matter. Next generation sequencing revealed two novel mutations in the galactosylceramidase (*GALC*) gene, and beta-galactocerebrosidase activity was reduced, confirming the diagnosis of Krabbe's disease.

Conclusion This case highlights an unusual presentation of Krabbe's disease with progressive hypertrophic polyradiculoneuropathy, associated with a novel genetic mutation.

059 TAKOTSUBO CARDIOMYOPATHY AND MYASTHENIC CRISES: A CASE SERIES

¹Matthew Katz*, ²Stephen Walsh, ³Benjamin Tsang, ¹Pamela McCombe, ²Arman Sabet. ¹Royal Brisbane and Women's Hospital, Brisbane, QLD, Australia; ²Gold Coast University Hospital, Gold Coast, QLD, Australia; ³Sunshine Coast University Hospital, Sunshine Coast, QLD, Australia

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Introduction Takotsubo cardiomyopathy (TCM) is an acute, reversible cardiomyopathy that can mimic acute coronary syndrome.¹ It is characterised by left ventricular dysfunction, electrocardiogram (ECG) changes and transient apical ballooning in the absence of significant coronary artery disease.¹ It is usually triggered by acute stress with catecholamine surge but the exact pathogenesis is not known.¹ Takotsubo cardiomyopathy

has been described in patients with myasthenic crisis. We present the first and largest case series of four patients with TCM in the setting of myasthenic crisis and discuss possible causes.

Methods Two patients from each tertiary neurologic centre were identified by their treating neurologist for inclusion in the series. We performed a review of their case notes with respect to history, examination, investigations and management. A brief literature review was also completed.

Results The mean age was 78 with a 1:1 female to male ratio. Three of the patients were newly diagnosed with myasthenia gravis (MG) at the time of their TCM. All patients were AChRab positive. One patient had a previous thymectomy but the others had no evidence of thymoma.

On review of the literature most cases of TCM in myasthenic crisis occurred in older females. Abnormalities of the ECG were universal. Most cases did not have a thymoma or history of thymectomy.

Conclusion Takotsubo cardiomyopathy may be easily overlooked in those presenting with myasthenic crises as they share overlapping clinical features. Rigorous attention to the cardiac status of these patients, especially the ECG, may help to avoid missing this important diagnosis.

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060 IMPAIRED COLOR DISCRIMINATION IS ASSOCIATED WITH HALLUCINATIONS IN DEMENTIA WITH LEWY BODIES

¹Elie Matar*, ²Joseph R Phillips, ¹Kaylena A Ehgoetz Martens, ¹Glenda M Halliday, ¹Simon JG Lewis. ¹Brain and Mind Centre, University of Sydney, Camperdown, NSW, Australia; ²MARCS Institute for Brain, Behaviour and Development, Western Sydney University, Sydney, NSW, Australia

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Introduction Emerging evidence indicates that color discrimination impairments can predict the development of dementia across a range of prodromal Lewy body conditions. However, color vision deficits are not seen uniformly in patients with Dementia with Lewy Bodies (DLB), suggesting a more nuanced association. Visual hallucinations (VH) represent a discriminating feature of DLB, and recent evidence implicates visual pathway dysfunction as a significant contributor to this phenomenon. We therefore hypothesized that color impairment will more closely associate with VH in DLB rather than general cognition.

Methods In this study, we examined the relationship between color vision impairment and VH, along with other clinical and neuropsychological features in 24 patients with DLB alongside 25 age-matched controls. Color discrimination was assessed using the Farnsworth-Munsell-100 Hue (FM-100) test.

Results Color discrimination impairment was seen in 16/24 DLB participants (67%) with a higher error score relative to controls ($p=0.001$). We demonstrate for the first time a strong association between color discrimination errors and both the presence and severity of VH in DLB based on clinician-derived ($p=0.008$) and questionnaire-derived ($p=0.03$) measures. Correlation with clinical and neuropsychological variables revealed that color discrimination is significantly