in this study. Eligible patients must have received a script for a reimbursed DMT for RRMS between September 2011 and February 2016. Patients were classified into five age-groups (ages 18–30; 31–40; 41–50; 51–60; 61+) and defined as persistent if their DMT script was filled within 4 months. Persistence was derived using the Kaplan-Meier method and hazard ratios (HR) to represent the relative rate of drop-off of different age groups.

Results Patients aged 18–30 (n=250) had a 44% increased risk of discontinuation (HR 1.44 [95%CI: 1.22–1.72]) compared to the ‘all ages’ cohort (n=1,866); no significant difference was observed for any other age group (HRs between 1.08 and 0.92). Patients in this 18–30 age-group had a significantly higher risk of discontinuation on injectable therapy (glatiramer acetate, interferon beta-1a, interferon beta-1b) compared to those on non-injectable therapy (dimethyl fumarate, fingolimod, natalizumab, teriflunomide) (HR 2.42 [95%CI: 1.63–3.61]).

Conclusions Patients aged 18–30 were the least persistent age group in this study. Patients aged 18–30 were less persistent on injectable than non-injectable DMTs.

051 OVERLAPPING SYNDROME OF GIANT CELL ARTERITIS AND ANCA-ASSOCIATED VASCULITIS COMPROMISED BY SEVERE AXONAL NEUROPATHY: A CASE REPORT

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Case A 61-year-old woman presented with what was thought to be a refractory, temporal artery biopsy-proven giant cell arteritis (GCA). After 4 months of therapy she was unable to get the prednisolone dose below 40 mg/day, so weekly subcutaneous Tocilizumab was introduced but with minimal response after 8 weeks. She was then admitted to hospital with a severe rapidly progressive length dependent sensorimotor peripheral neuropathy. Nerve conduction studies showed predominantly an axonal neuropathy with multiple pseudoconduction blocks.

Sural nerve and gastrocnemius biopsies revealed a necrotising vasculitis with numerous giant cells and active axonal degeneration. She proved to be ANCA-PR3 positive, without other systemic manifestations. ANCA-associated vasculitic neuropathy was diagnosed and she was treated with two 1g Rituximab infusions, 2 weeks apart.

On follow-up after a month, she had regained some strength but still required a wheelchair for mobility. Further Rituximab infusion after 6 months is planned; prednisolone had been successfully weaned to 10 mg/day.

Conclusion Peripheral nerve involvement, which is relatively common in ANCA-associated vasculitis, has also been reported in 14% of GCA cases. But ANCA-PR3 positivity is rare in biopsy-proven GGA, with only a handful of well-documented cases.

Heightened suspicion of an alternative diagnosis in the face of an unusual clinical course (lack of steroid response and appearance of small vessel vasculitic symptoms for what is accepted to be a large vessel vasculitis) is critical and our experience highlights the important fact that a diagnosis of one of these disorders does not preclude the subsequent diagnosis of the other.

053 GLUT-1 DEFICIENCY PRESENTING AS DOPA-RESPONSIVE DYSTONIA: AN ATYPICAL PHENOTYPE OF A RARE DISEASE

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Introduction The SLC2A1 gene encodes the glucose transporter GLUT1, responsible for normal glucose transport across the blood-brain barrier. Mutations in this gene have classically been associated with an epileptic encephalopathy referred to as GLUT-1 Deficiency Syndrome, which typically presents with early-onset refractory epilepsy, developmental delay and complex movement disorders.1 2 More recently, SLC2A1 variants have been identified in patients with paroxysmal exercise-induced dyskinesia (PED), with or without a history of epilepsy.3 4 Response to medication is typically poor; however, both seizures and dyskinesia may improve following implementation of a ketogenic diet.5 A single case of levodopa responsiveness has previously been described in a subject with SLC2A1 mutation and PED.5

Methods and results We describe a 47-year-old female with mild intellectual disability since childhood but no history of epilepsy, who developed episodic dystonia affecting the lower limbs in her early 20’s. A clinical diagnosis of dopa-responsive dystonia was made following a marked, sustained response to levodopa. There was no significant family history. In her 40’s she developed breakthrough dystonia with exertion and choreiform movements affecting the fingers and face. A subsequent dystonia panel identified a heterozygous variant c.[1199G>T]; [p.Arg400Leu] in the SLC2A1 gene. Cerebrospinal fluid glucose concentration was low (2.0 mmol/L). She declined a trial of a ketogenic diet.

SLC2A1 variants are associated with PED; however, response to levodopa has not been widely reported.

Conclusion It is becoming increasingly evident that the phenotypic presentations of GLUT1 deficiency are diverse, and SLC2A1 testing should be considered in a broader range of patients.

References

054 IMPACT OF ONLINE ADULT HEADACHE GUIDELINE ON HEADACHE REFERRAL TO NEUROLOGY CLINIC

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Introduction Headache is a common problem in primary care and is one of the main reasons for general practitioners to
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 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**

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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 severe pure motor axonal and lower motor neuron signs in bilateral upper and lower limbs. 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**

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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±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 (0.04–0.23) 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.