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

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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

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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.