Results Eighty-eight patients with POCI were included (median age: 69 with interquartile range [60- 78]; NIHSS at baseline: 8 [5–14]; DWI lesion volume: 3 [0.6–16] ml). Three-hundred-two patients were included in the reference group (median age: 72.5 [61–80.8]; NIHSS at baseline: 12 [6–17]; DWI lesion volume: 15.1 [3–50] ml). Optimal model performed was achieved using Delay Time (DT) maps with an accuracy of 0.89 (sensitivity: 0.77; specificity: 1). Mean Transit Time and Cerebral Blood Flow yielded lower but acceptable accuracies of 0.83 (sensitivity/specificity: 0.61/0.97) and 0.80 (sensitivity/specificity: 0.51/0.97), respectively.

Conclusions Classification of POCI using a CNN is highly accurate. Optimal model performance was achieved using DT maps. A CNN classification model may aid in the rapid and accurate diagnosis of POCI.

4 SERUM NEUROFILAMENT LIGHT CHAIN IN HEREDITARY TRANSTHYRETIN AMYLOIDOSIS: A VALIDATION STUDY

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Objectives Sensitive biomarkers of disease and progression are needed in hereditary transthyretin amyloidosis (ATTRv). Neurofilament light chain (NfL) has emerged as a potential biomarker, however, appropriate cut-off values, alteration longitudinally and applicability in real-world settings requires evaluation.

Methods NfL levels were measured longitudinally (2015–2022), in presymptomatic and symptomatic ATTR variant carriers. Correlations between NfL and demographics, renal function, examination, and staging scores were performed. ROC analyses were performed to determine cut-off values. NfL changes longitudinally were explored, pre-treatment, in asymptomatic and symptomatic cohorts, and converters to sensory or motor neuropathy via mixed-effect models.

Results 59 individuals with mixed ATTR variants (26=T60A, 12=V30M, 21=other [including G47V/V112I/S77Y/A97S]) and PND scores (0=18, 1=19, 2=9, >3=13) were studied over maximum follow-up of 4.75 years.

No correlations were found between NfL and age, creatinine, eGFR, gender or mutation. NfL correlated with CMTNS (r=0.56, p=0.002), NIS (r=0.5, p=0.0014), and MRC scores (r=-0.57, p<0.001). NfL significantly differed between PND0 and PND2, PND3A and PND3B (all p<0.003), and PND1 and PND3B (p= 0.047). NfL differed between FAP2 and FAP0 (p= 0.001) and FAP1 (p=0.03). Patients with PND>2, were discriminated from PND0–1, by NfL>52.2pg/ml (AUC=0.83; 95%CI:0.71–0.95; sensitivity=100%, specificity=55.5%).

NfL was higher in symptomatic and motor converters, than in asymptomatic or sensory converters, irrespective of time (all p<0.001). Symptomatic or motor converters were discriminated from asymptomatic by NfL>64.5pg/ml (AUC=0.95; 95%CI:0.90–0.99; sensitivity= 91.9%, specificity=88.5%).

Conclusions This study proposes NfL cut-off values for conversion to symptomatic disease and validates the use of NfL to monitor disease activity and progression in ATTRv.

5 AHSCT AS IMMUNE RECONSTITUTION THERAPY FOR MS – RESETTING THE IMMUNE SYSTEM OR DEPLETING EBV RESERVOIRS?

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Objectives It is established that autologous haematopoietic stem cell transplant (AHSCT) is a high-efficacy form of therapy for MS patients who have active disease despite pharmacotherapy; inducing protracted disease remission. Despite the import of EBV in MS pathogenesis no study has reviewed the effect of AHSCT on EBV viraemia, anti-EBV T and B cell immunity, nor latent viral load. Here, we study immune reconstitution which follows AHSCT to parse the role of EBV infection, anti-EBV immunity and its impact on MS.

Methods Bio-banked peripheral blood mononuclear cells (PBMCs) and platelet depleted plasma (PDP) were collected from MS patients enrolled in a phase 2 clinical trial (ACTRN12613000339752) pre-AHSCT, and at months 3, 6, 12, 24 and 36 post-AHSCT, n=22. Repertoire sequencing of TCRb chains were amplified from FAC-sorted CD4/CD8 naïve and memory cells. Longitudinal EBV-avid TCR responses were assessed through HLA-restricted repositories (VDJdb.com). EBNA IgG titres were analysed using the Abbott EBNA IgG kit. EBV viraemia and EBV genome load per cell was calculated using qPCR.

Results EBV DNAemia was rare beyond 3 months post-AHSCT, occurring in 3/22 individuals. DNAemia correlated with detectable EBV-specific T cell responses, clonal expansions of CD8+45RO+ T cells targeting both lytic and latent EBV epitopes. EBNA1 titres were preserved in 19 patients, and fell in 3 patients, all of whom relapsed post-AHSCT. EBV genome load within memory B cells increased concurrent with relapse in a single patient, 13 months post-AHSCT.

Conclusions Perturbations in EBV viral load and anti-EBV immunity appear to associate with relapse post-AHSCT.