EPR3101

CSF biomarkers do not associate to early disability in Multiple Sclerosis

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Introduction: Neurodegeneration occurs early in Multiple Sclerosis (MS), and caused clinical deterioration and disability. Biomarkers reflecting this phenomena, such as neurofilament light chain (NF-L), tau and β-amyloid (Aβ), could be measured easily in the cerebrospinal fluid (CSF).
Aim: To evaluate if CSF biomarkers of neurodegeneration predict early MS disability.
Methods: CSF NF-L, Aβ and tau levels were determined with commercial enzyme-linked immunosorbent assay in 48 newly-diagnosed MS patients (33 females). Baseline disease-courses were: three radiological (RIS) and 18 clinical isolated syndrome (CIS), 24 relapsing-remitting (RR) and 3 primary of secondary progressive (PR)-MS. Our disability outcome was the MS severity score (MSSS) at the last follow up (minimum 1 year after disease onset). We estimated differences between CSF biomarkers in baseline MS courses and disability with ANOVA.
Results: First, only CSF NF-L differed significantly among MS courses (p=0.002). In fact RIS showed the lowest levels (CSF NF-L mean 206 ng/ml±standard deviation 220) if compared to CIS (1158±511), RR (1616±741), and PR-MS (1714±27). On contrast, none of the CSF biomarkers was related to MSSS at last follow up. Of note, we excluded a correlation among tau or Aβ levels with NF-L.
Conclusion: NF-L are the unique biomarker of neurodegeneration related to MS forms. Their levels increased progressively with MS-course severity reflecting the higher axonal damage in PR-MS.
CSF NF-L, Aβ and tau failed to predict early MS disability: short-term outcome could not reflect the natural disease history.
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Lack of apparent association between lymphocyte pharmacodynamics and clinical or MRI disease activity in alemtuzumab-treated relapsing-remitting Multiple Sclerosis patients through 6 years: CARE-MS extension

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Background and aims: In the CARE-MS studies (NCT00530348; NCT00548405), alemtuzumab (12mg/day, baseline: 5 days; 12 months later: 3 days) significantly improved clinical/MRI outcomes versus subcutaneous IFNB-1a over 2 years in patients with active relapsing-remitting MS. Durable efficacy was observed in a 4-year extension (NCT00930553) without continuous treatment; 53% of patients received no additional alemtuzumab or other disease-modifying therapy. The effects of alemtuzumab may be due to its selective depletion and distinctive repopulation of circulating CD52-expressing T and B lymphocytes. We examine the association between lymphocyte repopulation patterns and clinical/MRI disease activity through 6 years following alemtuzumab treatment.
Methods: Blood counts were performed monthly; lymphocytes were phenotyped by flow cytometry quarterly and at Months 1 and 13. Lymphocyte subset counts from the CARE-MS studies were pooled (CD4+/CD8+ T-cells: total/naïve/memory/regulatory [Treg]; CD19+ B-cells: total/immature/mature/memory). Further analyses examined ratios of CD19+ (total/immature/memory) to Treg (CD4+/CD8+) cell counts. Relationship between lymphocyte repopulation patterns and efficacy was assessed in patients with/without relapses, 6-month confirmed disability worsening (CDW; ≥1.0-point Expanded Disability Status Scale increase [≥1.5 points if baseline EDSS=0]), or MRI disease activity (new gadolinium-enhancing lesions or new/enlarging T2 lesions).
Results: Lymphocyte subset repopulation kinetics over 2 years did not differ in patients with or without relapses, CDW, or MRI disease activity through 6 years. No correlation was observed between any CD19+/Treg cell count ratio and relapse, CDW, or MRI disease activity.
Conclusion: Based on these analyses, lymphocyte repopulation kinetics were not associated with return of disease activity and likely cannot be used to predict need for further treatment.
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