Fluid biomarkers (CSF/Blood) in AD and VCI

노 영
가천의대

Young Noh, MD, PhD
Department of Neurology, Gachon University Gil Medical Cennter, Incheon, Korea

Identification of reliable biomarkers in biological fluids such as CSF or blood is of extreme importance in optimizing the precise early diagnosis of distinct disease entities and predicting the disease progression.

CSF and blood biomarkers for the diagnosis of Alzheimer's disease (AD) could be categorized as 1) core biomarkers such as total tau (T-tau), phosphorylated tau (P-tau) and Aβ peptides. 2) proteins related to synaptic degeneration or neuronal injury such as neurofilament light (NFL), YKL-40, neurogranin (Ng), NSE, VLP-1, HFABP etc. 3) neuroinflammation markers, and 4) miRNA or metabolomics. The core biomarkers (CSF T-tau, P-tau, and Aβ42) differentiated AD from controls with good performance. Differentiation between cohorts with mild cognitive impairment (MCI) due to AD and those with stable MCI was also strong for CSF T-tau, P-tau, and Aβ42. Furthermore, CSF NFL and plasma T-tau had large effect sizes when differentiating between controls and patients with AD, whereas those of CSF NSE, VLP-a, HFABP, and YKL-40 were moderate. Other assessed biomarkers had only marginal effect sizes or did not differentiate between control and patient samples.

CSF tau, P-tau and Aβ peptides have been proposed as helpful in discriminating among vascular dementia (VD), AD and controls. However, major differences reported among different studies impeded the use of CSF or blood-based biomarkers for the differential diagnosis of VD forms. This is largely due to heterogeneity of VD. Data on single biomarkers in VD are largely dependent on the population analysed, pointing up to the presence of high disease heterogeneity influenced by the presence of comorbidities, the type of vascular pathology and disease severity.

Compared with CSF markers, validated blood-based AD markers would provide a fast, noninvasive and cost-effective methods of early detection and diagnosis of the most common age-related neurodegenerative disease. As venipuncture is a routine, safe procedures, in contrast to CSF sampling, examination of blood biomarkers is accepted and easily introduced in the clinical environment. However, identification of potential blood-based biomarkers for CNS diseases presents several challenges. Blood is highly complex and includes a range of different molecules, which can be detected in plasma, exosomes and cellular components. The CNS is effectively a contained environment, and potential biomarkers might be present at very low concentrations in blood once they have crossed the blood–brain barrier. So, evidence for peripheral manifestations of AD is limited. To overcome these challenges, various attempts have been tried. Validations of fluid-based modalities were tried to achieve in comparison with advanced molecular neuroimaging techniques, including amyloid or tau PET. Development in research laboratory technologies, such as ultra-sensitive methods, raises our hope to further improve analytical and diagnostic accuracy of classic and novel candidate biomarkers.

Key Words: biomarker, CSF, blood, Alzheimer's disease, vascular cognitive impairment