„Ocena przydatności białek stanu zapalnego w diagnostyce choroby Alzheimera"

ABSTRACT

Alzheimer's disease (AD) is one of the most common causes of dementia in Poland and worldwide. Despite significant progress in the diagnosis of neurodegenerative diseases, there is still a lack of specific biomarkers that would reflect the molecular mechanisms of this disease. Although the etiology of Alzheimer's disease has not yet been fully explained, several key factors have been identified that significantly affect its development. The characteristic histopathological features of AD include extracellular amyloid plaques composed of amyloid β and fibrillary tangles, the basis of which is hyperphosphorylated tau protein.

Despite existing data in the literature on the role of neuroinflammation in the pathogenesis of AD, there are currently no studies assessing the relationship between the concentration of inflammatory proteins in the continuum of amyloid beta pathology or Tau protein, and analysis of changes in the concentrations of the above-mentioned proteins depending on the stage of disease development. Hence, the aim of this dissertation was to investigate selected proteins associated with the inflammatory process (pro- and anti-inflammatory) in patients with cognitive impairment (including Alzheimer's disease (AD) and mild cognitive impairment (MCI)) in relation to the concentrations of these proteins in the group of people without cognitive impairment, as well as to compare the concentrations of the studied proteins with indicators of the severity of cognitive impairment and concentrations of classic AD biomarkers in different stages of the disease, as well as to analyze the clinical usefulness of the studied proteins as potential biomarkers that may be used in the diagnosis and assessment of AD progression.

Glycoprotein, non-metastatic melanoma protein B (GPNMB), YKL-40, neutrophil gelatinase-associated lipocalin (NGAL), CXCL-11, sTREM1 and sTREM2 were assessed using immunological methods (i.e. classical ELISA method and xMAP multiplexing technology on the Luminex 200 platform) in the cerebrospinal fluid (CSF) of patients with MCI, AD and control subjects without cognitive impairment.

The conducted studies have shown that the developing inflammation and the associated increase in the concentration of proteins such as GPNMB, NGAL and CXCL11 already in the early stages of the disease (MCI stage) may be one of the key mechanisms promoting disease progression. Moreover, the better diagnostic utility of GPNMB (AUC value) observed in the early stages of AD development compared to amyloid protein and the increased concentration of GPNMB in the Aβ (+) group indicate the potential diagnostic utility of this protein in AD. Monitoring the dynamics of changes in the concentrations of inflammatory proteins released from neutrophils (NGAL, CXCL11) combined with the assessment of classic biomarkers in

patients with MCI may allow for the improvement of early diagnosis of Alzheimer's disease, while in the advanced stage of the disease, the activation of anti-inflammatory proteins (i.e. GPNMB, sTREM2) seems to be a key protective mechanism against the development of Tau protein pathology.

9.12.2024 Julia Dabrowska