J Neurol Neurosci, 8:5
DOI: 10.21767/2171-6625-C1-003

The role of the lymphatic system in the development of brain amyloidosis

Miguel Pappolla
St. Michael's Pain and Spine Clinics, USA

Alzheimer's disease (AD) is characterized by brain deposits of a mostly 40 to 42 amino acid peptide, the amyloid β protein (Aβ), in senile plaques and intracranial blood vessels. Aβ exhibits a strong tendency to aggregate into neurotoxic oligomeric forms. The "amyloid hypothesis" of AD proposes that elevated levels of Aβ oligomers trigger a downstream cascade of oxidative and pro-inflammatory events which lead to the widespread death of neurons and dementia. It has been postulated that inadequate clearance of the amyloid β protein (Aβ) plays an important role in the accumulation of Aβ in sporadic late onset AD. While the blood brain barrier (BBB) has taken the center stage in this field, little information is available about the role of the lymphatic system in Aβ clearance. We previously reported that Aβ is cleared through the lymphatic system. We now assessed lymphatic Aβ clearance by treating a mouse model of AD amyloidosis with melatonin, an Aβ aggregation inhibitor and immuno-regulatory neurohormone. We examined Aβ levels in plasma and in lymph nodes of transgenic mice as surrogate markers of vascular and lymphatic clearance, respectively. Treatment with melatonin led to the following changes: 1-A *statistically significant* increase in soluble monomeric Aβ40 and an increasing trend in Aβ42 in *cervical and axillary lymph nodes* of treated mice. 2-*Statistically significant* decreases in oligomeric Aβ40 and Aβ42 in the brain. 3-Lack of changes of Aβ40 and Aβ42 levels in plasma with aging. 4-Elimination of premature mortality in transgenic mice. Several mechanisms involving the lymphatic system in the clearance of cell debris and waste solutes, including amyloid, from the mammalian central nervous system will be discussed. These include lymphatic clearance pathways along cranial nerves, spinal nerves, the cribriform plate, meningeal lymphatic channels and paravascular pathways including the glymphatic system. In addition to the pathways of clearance mentioned here, it is likely that active cellular transport mechanisms are in play. For example, the murine PirB (paired immunoglobulin-like receptor B) and its human ortholog LilrB2 (leukocyte immunoglobulin-like receptor B2), present in human brain, are receptors for Aβ peptides. These receptors, which are members of the immunoglobulin superfamily, are found in dendritic cells. These cells are known to "travel" between brain and lymph nodes. The data that will be presented suggest that abnormalities in the clearance through the lymphatic system may contribute to the development of brain amyloidosis.

e: papppolla@aol.com

Notes: