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Tissue Reactions to CAA Study using Tissue Microarrays (CNS Complications of Amyloid Angiopathy)

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Project description

Cerebral congophilic or amyloid angiopathy (CAA) is a common microvascular abnormality in the brains of elderly patients, especially those with Alzheimer disease (AD). Though it occurs in the brains of neurologically normal elderly patients, as do senile plaques and neurofibrillary tangles, CAA is most severe and most often symptomatic (sometimes producing primary intraparenchymal cerebral hemorrhage) in the brains of patients with AD.

CAA is characterized by the accumulation within capillary and arteriolar walls of fibrillar A and gamma-trace/cystatin C proteins, which (as they are deposited) cause degeneration of arteriolar smooth muscle cells, with resultant weakening of the affected vessel wall. The effects of progressive CAA on surrounding brain parenchyma (other than the comparatively rare occurrence of intraparenchymal hemorrhage) have not been systematically studied. This multi-Center project will define brain parenchymal abnormalities that may result from variably severe meningocortical CAA (especially affecting subcortical white matter), using an immunohistochemical and morphometric approach.

This study involves collection of 200 AD cases, 60 from each participating Center (20 each from three CAA severity levels), and 20 additional cases from UCLA with no CAA. Extensive use will be made of tissue microarrays constructed by systematically sampling multiple brain regions (from appropriate autopsy samples) and performing quantitative analysis of these ‘tissue chips’ using a variety of probes and immunoreagents.

Brain parenchymal reactions that may contribute to cognitive impairment in affected individuals, e.g. proliferation of microglia and astrocytes, and degeneration of subcortical white matter (including apoptosis of oligodendroglia), are being assessed. Co-morbidity involving both CAA and cerebral arteriosclerosis are being evaluated. This represents the first attempt to understand the potential impact of CAA — the amyloid lesion from which A peptide was initially isolated — on adjacent CNS parenchyma.

Contact information

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