Cerebrovascular abnormalities in Alzheimer's disease

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Cerebrovascular changes are not exclusive to vascular dementia (VaD) or multi-infarct dementia. Our previous observations in a large autopsy series of cases have shown profound brain microvascular lesions in Alzheimer's disease (AD). It is not unlikely that the microvascular changes are compounded by the presence of cerebral amyloid angiopathy (CAA). Amyloid β (Aβ) type of CAA has been the most investigated in view of its enhanced presence in the elderly and in greater than 90% of Alzheimer's disease and Down's syndrome. In our series vascular pathology comprised intense deposition of fibrillar amyloid in walls of vessels in the leptomeninges, perforating arteries, intraparenchymal arterioles as well as focal deposits in capillaries associated with degeneration of both vascular smooth muscle and endothelium in vessel profiles. However, AD pathology was also associated with microinfarcts and to lesser extent large infarcts and CAA-related intracerebral haemorrhages. We suggest vascular tone and blood-brain barrier function albeit locally are likely to be profoundly impaired in affected cerebral vessels. Evidence also suggests that angiopathy per se is a substrate for dementia. Other features include periventricular and deep white-matter changes or leukoariaosis seen upon magnetic resonance imaging and at autopsy in more than 40% of the late-onset AD cases. Such brain vascular pathology in AD may arise from systemic vascular or cardiovascular disease. Alternatively, VaD patients bear AD-type of pathology at autopsy and these also reveal neurochemical abnormalities consisting of deficits in presynaptic cholinergic indices related to the basal forebrain neurones. We also noted Abeta deposits and tangles were present in 43% of VaD patients with a small volume (<15 ml) of macro-infarction. These findings corroborate the importance of microvascular disease rather than macroscopic infarction as the critical substrate in VaD and also implicate cholinergic deficits in VaD. Is it possible that the microvascular lesions or multiple mircoinfarcts are the underlying primary trigger for subsequent Alzheimer pathology in late-onset AD? Evidence to implicate neovascularisation in AD pathogenesis will also be reviewed. Treatment strategies that improve the dynamics of the cerebral circulation and chronic hypoperfusion would be rational targets for dementia.

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