Vascular Contributions in Alzheimer’s Disease-Related Neuropathological Changes: First Autopsy Evidence from a South Asian Aging Population

Printha Wijesinghe, S.K. Shankar, T.C. Yasha, Catherine Gorrie, Dhammika Amaratunga, Sanjayah Hulathduwa, K. Sunil Kumara, Kamani Samarasinghe, Yoo-hun Suh, Harry W.M. Steinbusch and K. Ranil D. De Silva

Interdisciplinary Center for Innovation in Biotechnology & Neuroscience, Genetic Diagnostic and Research Laboratory, Department of Anatomy, Faculty of Medical Sciences, University of Srijayewardenepura, Nugegoda, Sri Lanka

Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore, India

School of Medical and Molecular Biosciences, University of Technology Sydney, Sydney, Australia

Nonclinical Biostatistics, Janssen Research & Development, Raritan, NJ, USA

Department of Forensic Medicine, Faculty of Medical Sciences, University of Srijayewardenepura, Nugegoda, Sri Lanka

Department of Judicial Medical Office, Colombo South Teaching Hospital, Colombo, Sri Lanka

Department of Pathology, University of Srijayewardenepura, Nugegoda, Sri Lanka

Department of Pharmacology, College of Medicine, Seoul National University, Seoul, Korea

NRI, Gachon University, Incheon, South Korea

Department of Translational Neuroscience, Faculty Health, Medicine & Life Sciences, Maastricht University, Maastricht, Netherlands

Handling Associate Editor: Ignacio Casado Naranjo

Accepted 15 July 2016

Abstract

Background: Evidence from various consortia on vascular contributions has been inconsistent in determining the etiology of sporadic Alzheimer’s disease (AD).

Objective: To investigate vascular risk factors and cerebrovascular pathologies associated in manifestation of AD-related neuropathological changes of an elderly population.

Methods: Postmortem brain samples from 76 elderly subjects (≥50 years) were used to study genetic polymorphisms, intracranial atherosclerosis of the circle of Willis (IASCW), and microscopic infarcts in deep white matters. From this cohort, 50 brains (≥60 years) were subjected to neuropathological diagnosis using immunohistopathological techniques.
Results: Besides the association with age, the apolipoprotein E e4 allele was significantly and strongly associated with Thal amyloid-β phases ≥1 [odds ratio (OR) = 6.76, 95% confidence interval (CI) 1.37–33.45] and inversely with Braak neurofibrillary tangle (NFT) stages ≥III (0.02, 0.0–0.47). Illiterates showed a significant positive association for Braak NFT stages ≥IV (14.62, 1.21–176.73) and a significant negative association for microscopic infarcts (0.15, 0.03–0.71) in deep white matters. With respect to cerebrovascular pathologies, cerebral small vessel lesions (white matter hyperintensities and cerebral amyloid angiopathy) showed a higher degree of associations among them and with AD-related neuropathological changes (p < 0.05) compared to large vessel pathology (IASCW), which showed a significant association only with Braak NFT stages ≥I (p = 0.050).

Conclusion: These findings suggest that besides age, education, and genetic factors, other vascular risk factors were not associated with AD-related neuropathological changes and urge prompt actions be taken against cerebral small vessel diseases since evidence for effective prevention is still lacking.

Keywords: Alzheimer’s disease, apolipoprotein E, atherosclerosis, cerebral small vessel diseases, neuropathology