Large vessel, small vessel and smallest vessel brain disease – their different contribution to neurodegeneration

Bogdan O. Popescu, MD, PhD

Department of Neurology, Colentina Clinical Hospital

‘Carol Davila’ University of Medicine and Pharmacy, Bucharest, Romania

The net effect of neurodegeneration is loss of neurons and loss of neurologic functions and abilities. Two great health enemies affect us all at the highest possible level in respect to neurodegeneration processes – age and vascular disease, which actually progress hand in hand.

Significant atheromatosis starts both to limit the blood supply to the brain and develop the necessary background for thrombosis and arterial emboli. This large vessel disease decrease the cerebral blood flow (CBF) and alter the function of neurovascular unit, resulting in a decreased neurovascular coupling (reduced reaction of blood flow increase in cortical areas in neuronal function activation situations), which corresponds clinically to decreased performance. Advanced cerebral large vessel disease also leads to large brain infarcts which take away specific brain volumes, disconnecting the brain not only vertically but also horizontally, fact which is rarely considered and analyzed. However, from different studies it looks like large ischemic lesions on one hand might aggravate neurodegenerative pathology in vicinity areas but also might wake up dormant neural stem cells, located mainly to related meninges and choroid plexus.

A completely different mechanism is linked to small artery disease, which lead to lacunar infarcts and diffuse white matter alterations. Lacunar lesions occur mainly in the basal ganglia and thalamus, taking away loops of the ubiquitous cortico-striato-thalamo-cortical circuits and wide spread axonal lesions affect also this loops but also descending, ascending and horizontal brain connections. With the same beta-amyloid and tau cortical AD pathology load, brains with basal lesions perform worse in perfusion and metabolism studies and also in neuropsychological tests.

Last but not least comes the alteration of capillaries and of blood brain barrier properties. This yet uncovered pathology can be called the smallest vessels disease and there are quite numerous studies now showing that this smallest vessels can be altered in the absence of large or small demonstrable pathology. Vascular risk factors such as hypertension or diabetes are able to alter regulation of through BBB transport and to affect neurovascular coupling. Even not yet fully demonstrated but only in animal models, it might be possible that early BBB properties alteration to accelerate neurodegeneration progression.

Veins are another important but much less studied segments of brain vasculature. Different segments of brain veins seem to be pathologically changed by both arterial disease and by neurodegeneration. Choroid plexus might have a role in regulating neurogenesis and it was not studied in relation with hallmark pathologic markers of neurodegeneration.
Even though common vascular risk factors, such as hypertension, diabetes or dyslipidemia could affect all vascular segments, the contribution of each of these lesions to promotion of neurodegeneration seems to operate through different pathogenic mechanisms.