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Complexity of damage-associated molecular pattern molecules (DAMPs) expression profile in porcine brain affected by ischemic stroke

Abstract: Ischemic stroke is one of leading causes of death worldwide. Cerebral ischemia resulting from infarction of one of the arteries supplying the brain leads to a cascade of inflammatory reactions initiated by increased release of danger/damage-associated molecular patterns (DAMPs), which, acting through receptors on microglia and astrocytes, induce increased cytokine production and infiltration of immune cells from the periphery. The aim of our study was to determine the relationship between different DAMPs in the porcine brain after ischemic stroke and to evaluate the time points of inflammatory reactions. We determined increased expression of proinflammatory cytokine genes: IL1A and IL1B, TNF α 6 h after stroke induction. This indicates an intense and strong inflammatory reaction in the hyperacute phase of ischemic stroke, which is most likely related to the passive release of DAMPs by necroptotic neuronal cells. Increased expression of HMGB1, TLR4 and NF κ B1 was observed in the subacute phase, one week after stroke onset. This may be related to the ongoing inflammation and the recruitment of immune cells, as well as to the beginning of vascular remodeling in the affected area. In turn, an increased expression of CD39 and CD73 genes one week after cerebral ischemia in pigs and the consequent elevation in extracellular adenosine attenuate the inflammatory response, playing a neuroprotective role. In summary, our studies have for the first time determined and systematized the importance and complexity of DAMP action after cerebral ischemia in pigs and highlighted their dual role. The complexity of their action is particularly visible at the beginning of the subacute phase, where – according to the results of our studies – the inflammatory reaction, initiation of angiogenesis and partial neuroprotection can occur simultaneously.

Keywords: Stroke, Animal model, DAMPs, Pig, Brain

Biography: Izabela Małysz-Cymborska has been an associate professor at the Department of Neurosurgery at the Faculty of Medicine of the University of Warmia and Mazury in Olsztyn since 2022. She obtained her PhD at the Institute of the Polish Academy of Sciences in Olsztyn in 2015. For almost a decade, her work has focused on modeling neurological disorders in small and large animals, including ALS, stroke or GBM. She introduced an innovative method of culturing stem cells in a 3D system using alginate hydrogels, enabling their imaging in magnetic resonance imaging. She describes herself briefly as a scientist by passion, a biologist by choice.