DOI 10.36074/logos-19.03.2021.v4.02

PHAGOCYTOSIS ACTIVATION IN THE RAT BRAIN IN THE CONDITIONS OF ACUTE SOMATOGENIC TOXIC ENCEPHALOPATHIES

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Currently sepsis and liver failure are the most often reasons of the endogenous intoxication which causes damage of the brain and toxic encephalopathy. The sepsis-associated encephalopathy (SAE) can result in cognitive alterations up to coma. Acute hepatic encephalopathy (AHE) manifests also as acute cerebral dysfunction and usually occurs in severe form, accompanied by cytotoxic brain oedema. The mechanisms of SAE and AHE are to be elucidated, but the common links in their development are microglial activation and neuroinflammation [1]. In is considered that in case of systemic inflammation microglia transform to the neurotoxic phenotype and produce proinflammatory cytokines supporting uncontrolled neuroinflammation [2]. Given the identified morpho-functional heterogeneity of the microglia [3], more detailed research of the microglial activation in different brain regions would be useful for understanding mechanisms of the cerebral dysfunction in the conditions of sepsis and acute liver failure. The purpose of the study was analyzing immunohistochemical (IHC) specificity of the microglial reactivity in different brain regions in the conditions of experimental SAE and AHE. The study was conducted in Wistar rats, which were subjected to cecal ligation and puncture (CLP) model of sepsis and acetaminophen induced liver failure (AILF) model of AHE [1]. Microglial activation was determined by IHC evaluation of the expression of CD68 in the cortex, white matter, hippocampus, thalamus, caudate/putamen in the relative area (S rel., %) of $CD68^+$ and $CD68^+$ cell numbers. In the CLP-group survived animals (CLP-A) showed moderate, reliable, regional-specific increase in indicators of microglial activation in the brain by 48 h. Statistically significant differences of the parameters were characteristic for: cortex, subcortical white matter, hippocampus, and caudate/putamen. In the non-survived CLP-B group, the most significant increase in all parameters was observed with the highest values in descending order: white matter, caudate/putamen, hippocampus and cortex. In the thalamus of both groups an increase was not statistically significant. In the AILF-model the survived AILF-A animals by 24 h of the experiment also showed moderate increase in signs of microglial activation in the brain, although less prominent. The statistically reliable indicators of the S rel. of $CD68^+$ and numbers of CD68+-cells were typical for subcortical white matter and caudate/putamen but not for cortex, thalamus and hippocampus. Non-survived animals demonstrated increase in two studied parameters in subcortical white matter, thalamus and caudate/putamen, except cortex and hippocampus. Thus, in the conditions of SAE and AHE in the rat brain there is region-specific signs of microglial activation. SAE is characterized by pronounced increase of the parameters in the white matter, caudate/putamen, cortex and hippocampus, while AHE demonstrated increased microglial reactivity predominantly in white matter, caudate/putamen and thalamus

(in non-survived animals). The revealed specificity most likely may indicate the brain regions with the most active neuroinflammatory response occur in the conditions of acute hepatic and sepsis-associated encephalopathy.

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