MODERN UNDERSTANDING OF CEREBRAL EDEMA IN THE ACUTE PERIOD OF TRAUMATIC BRAIN INJURY AND IN ACUTE CEREBROVASCULAR ACCIDENTS (LITERATURE REVIEW)

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Abstract: Cerebrovascular diseases are one of the most serious medical and social problems in the world today. According to the World Health Organization (WHO) in 2013, about 6.2 million people die annually from stroke or cerebrovascular diseases (10.8% of the total number of deaths). Mortality ranks second after cerebrovascular diseases after heart disease and is 8% in men and 16% in women. This disease affects middle-aged people, reduces their ability to work, leads to disability and increases the number of deaths. Despite the fact that new methods of diagnosis and treatment of stroke are being developed, mortality from this disease is growing throughout the world. The basis for the development of the main pathophysiological syndromes that occur in acute diseases and injuries of the brain (cerebral edema, dislocation syndrome, increased intracranial pressure) is hypoxia, which triggers a cascade of biochemical reactions that aggravate the phenomena of ischemia.

Key words: cerebral edema, dislocation syndrome, increased intracranial pressure.

Literary sources indicate that in response to traumatic brain injury, a complex of biochemical and pathophysiological reactions is triggered, determining the occurrence of certain clinical manifestations of TBI. One of these mechanisms is the immunological response to injury, which is accompanied by a change in the ratio of T-helper subpopulations and their functions, the degree and nature of which is manifested depending on the severity of the patient's traumatic brain injury.

T cells play an important role in the development and maintenance of secondary damage after brain injury through the interaction of different cell types. Thus, for the acute period, the phenomenon of the "critical period" is known, when the number of T-helpers becomes lower than the level of cytotoxic T-lymphocytes. These characteristic changes underlie the so-called initial mechanism of immunoregulatory disorders, which is expressed by inflammatory complications (Norka A.O., Vorobyov S.V., Emelin A.Yu. 2020).

In this inflammation, within 1–5 days after TBI, T-lymphocytes from the peripheral blood begin to penetrate into the nervous tissue, promoting the development of immune-mediated reactions. Important data in this case is that in most

neuroinflammatory diseases, in the foci of nervous tissue damage, clusters of CD3-positive lymphocytes are found that are capable of expressing the IL-17 gene and synthesizing this cytokine, associated with inflammatory and autoimmune reactions [Tzartos J.S. et al. 2008). At the same time, the subtle mechanisms of T-helper functioning and their role in the pathogenesis of diseases accompanied by the formation of an inflammatory reaction remain the subject of discussion in the press and various forums. New methods proposed recently allow us to significantly expand the possibilities of knowledge and solve a number of problems that have arisen.

Authors from St. Petersburg (Norka O.O. et al. 2023) consider the "inflammatory" mechanism of Th17, based on the effective clearance of the inflammation focus due to the introduction of neutrophilic granulocytes from the peripheral blood, to be an adequate and compensatory reaction of protective immunity. In their study, the scientists reveal the interactions between Th1 and Th17, as well as other cells of the immune system in patients with TBI, and propose new approaches to reducing the inflammatory process and enhancing tissue repair processes. The results obtained provide an opportunity to develop new therapeutic options for the treatment of TBI using immunotropic drugs.

It is also important to analyze the cellular and molecular mechanisms of development of post-traumatic complications. Research in this area will help to identify not only promising prognostic biomarkers, but also to determine new targets for therapeutic interventions.

Johnson NH, Hadad R, Taylor RR (2022) Traumatic brain injury is a complex and chronic pathology that represents a major public health problem in the United States and worldwide. According to the authors, there are 3.17 million people in the United States who suffer long-term disability due to TBI, representing an annual economic impact exceeding US$56 billion. TBI manifests as a biphasic pathology in which the effects of the initial traumatic insult lead to persistent inflammation and chronic activation of the innate immune system. The initial injury involves the release of damage-associated molecular patterns (DAMPS) from injured tissue, leading to activation of the innate immune response and formation of the inflammasome. Although DAMP and PAMP levels have been shown to gradually decline over the first week after injury, chronic inflammatory activity is often observed for months to years after injury, leading to secondary injury of chronically activated microglia and subsequent release of inflammatory cytokines. The authors propose a systematic approach to identify inflammatory biomarkers that includes:

(1) measuring the levels of inflammatory problems in the serum of affected and unaffected individuals to determine if there are statistical differences between the groups;

(2) to determine diagnostic biomarker characteristics (AUC, sensitivity,

specificity, likelihood ratio, accuracy, PPV, and NPV) of each inflammatory protein or analyte that were statistically significant when comparing levels between affected and unaffected individuals;

(3) comparison of ROC among different biomarkers to identify potential differences in biomarkers between groups;

(4) dichotomizing the GCS into mild and moderate and severe outcomes to determine the presence of inflammatory biomarkers that meet criteria as useful biomarkers of injury severity;

(5) dichotomizing the GOS-E into favorable and unfavorable outcomes to determine the presence of inflammatory biomarkers that meet criteria as useful biomarkers of long-term outcomes.

Johnson NH. Et al. identified caspase-1, ASC, IL-18, TNF-α, IL-2, IL-4, IL-6, IL-8, IL-10, and IL-12 as surrogate serum biomarkers of the acute inflammatory response after TBI. And the use of inflammatory biomarkers in combination with GFAP and UCH-L1 may give clinicians a better understanding of the overall extent of injury and provide probable prognosis and disability potential given the various mechanisms contributing to TBI pathology, including neuronal injury (UCH-L1), reactive astrogliosis (GFAP), and inflammation (caspase-1, ASC, TNF-α, and IL-6). Identification of clinically relevant biomarkers of the inflammatory response after TBI allows future studies to examine how therapeutic agents affect these biomarkers and how the effects of these agents on biomarkers influence injury severity and functional outcomes in patients after TBI.

Furthermore, the identification of these inflammatory biomarkers provides an opportunity to develop therapeutics that can be used to more specifically treat the inflammatory response associated with TBI. When combined with modern approaches to measure biomarkers with greater accuracy and sensitivity than in the past, as well as the identification of biomarkers of neuronal injury, reactive astrogliosis, and inflammation, personalized care for patients with TBI is becoming an increasingly tangible reality. Furthermore, in light of the results of this project, future studies in clinically relevant animal models of TBI should focus on understanding the individual and synergistic effects of therapeutic targeting of inflammatory proteins identified as relevant biomarkers of the inflammatory response following TBI for their ability to improve histopathological and functional outcomes.

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