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IMMUNOHISTOCHEMICAL CHARACTERISTICS OF THE ADRENAL GLANDS IN NEWBORNS WITH BIRTH-RELATED BRAIN INJURY

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Abstract. The development of criteria for assessing the morphofunctional status of the adrenal glands during the early period of birth-related brain injury is of considerable importance for evaluating the evolving pathomorphological changes. Such criteria, based on retrospective analysis, may enable prospective prediction of disease progression and contribute to the prevention of anticipated severe complications. Accordingly, when major tissue damage and hemorrhages predominate in birth-related brain injury and cerebral edema develops, a marked increase in glucocorticoid production by the adrenal glands may occur. The severity of adrenal involvement is considered highest when microscopic foci of hemorrhage are detected in two or more areas of both the adrenal cortex and medulla.

Keywords: assessment of adrenal gland injury, morphology, birth-related brain injury, necrosis, dystrophy.

Relevance of the Problem. Birth-related injuries in newborns, particularly birth-related brain injuries, represent an important cause of perinatal morbidity and mortality and remain a significant problem in modern neonatology. According to epidemiological studies, the reported incidence of birth-related injuries varies considerably, ranging from 0.2 to 41.2 cases per 1,000 live births, depending on geographical region, gestational age, characteristics of labor and delivery, and the clinical condition of the newborn. Birth-related brain injury may result in severe neurological impairment and can contribute to adverse neonatal outcomes, particularly when accompanied by perinatal asphyxia, hypoxic-ischemic injury, or mechanical trauma. The World Health Organization identifies intrapartum-related complications, including birth asphyxia and birth trauma, among the major causes of neonatal mortality, together with prematurity, infections, and congenital anomalies.

The clinical and morphological consequences of birth-related brain injury are particularly important during the early neonatal period, when hypoxia, impaired cerebral and systemic circulation, and hemodynamic disturbances may lead to secondary injury of vital organs. Therefore, the study of birth-related brain injury and its systemic consequences remains an important area of contemporary neonatology and perinatal pathology.

In this context, investigation of the morphological changes associated with birth-related brain injury is of particular scientific and practical importance. A better understanding of

these changes may contribute to more accurate assessment of disease severity, prediction of adverse outcomes, and improvement of approaches to the prevention of severe complications in newborns.

Materials and Methods. The study material consisted of adrenal gland tissue specimens obtained during autopsy from 69 full-term newborns who died as a result of birth-related brain injury. The morphological characteristics of adrenal gland tissue samples were examined.

Discussion and Results. To investigate the immunohistochemical characteristics of the adrenal glands in newborns who died as a result of birth-related brain injury, the HSP70 marker was used. HSP70 is a heat shock protein that is expressed predominantly in response to various stressors and contributes to the cellular stress response. Its expression may reflect the intensity of cellular stress and adaptive mechanisms in adrenal cortical cells. HSP70 is a 70-kDa protein involved in cellular responses to a wide range of stress conditions, including heat shock, traumatic shock, cardiogenic shock, infectious-toxic shock, and other adverse stimuli. Its expression is mainly observed in the cytoplasm of cells and is associated with multiple biological processes, including protein folding, cellular stress adaptation, apoptosis, neurodegeneration, and other cellular regulatory mechanisms.

Group 1 (0–8 hours). This period represented the early adaptive stress-response and protective phase. The previously identified morphological and morphometric changes differed from the control group by approximately 10–15%. Immunohistochemical examination demonstrated a marked increase in HSP70 expression, reaching high intensity. Among the 16 cases examined in Group 1, high-positive HSP70 expression was detected in 14 cases (87.5%), while moderate-positive expression was observed in 2 cases (12.5%). These findings indicate that compensatory mechanisms were highly active during the early phase of the pathological process.

From a clinical and morphological perspective, the findings suggest that delayed medical intervention in newborns with birth-related brain injury may contribute to the development of irreversible changes in the brain and internal organs. The observed HSP70 expression pattern corresponds to a period characterized predominantly by compensatory and subcompensatory responses of the adrenal glands.

Group 2 (8–16 hours). During the 8–16-hour period, the adrenal response to birth-related brain injury appeared to be associated with the duration and severity of the pathological process. Progressive depletion of intracellular resources, a marked reduction in the synthesis of adaptive hormones, intracellular structural disruption, and severe dystrophic changes were accompanied by a decrease in stress-related protein production and, consequently, reduced HSP70 expression. Among the 16 cases examined in this group, low-positive HSP70 expression was detected in 11 cases (68.75%), moderate-positive expression in 3 cases (18.75%), and a negative reaction in 2 cases (12.5%). The variability in HSP70 expression suggests that the adrenal response is not uniform and may depend on the duration

of the pathological process and the severity of brain injury associated with birth-related trauma.

Thus, the low- and moderate-intensity HSP70 expression observed in Group 2 may indicate that the surviving adrenal cells remain in a state of subcompensation, despite the progression of structural and functional disturbances.

Group 3 (16–24 hours). During the 16–24-hour period, newborns with birth-related brain injury demonstrated pronounced suppression of adrenal morphofunctional activity, accompanied by only focal and isolated areas of detectable HSP70 expression. These findings were consistent with the results of morphological and morphometric examinations. Destructive changes were observed in both the adrenal cortex and medulla. Among the 16 cases examined in Group 3, a negative HSP70 reaction was observed in 10 cases (62.5%), low-positive expression in 4 cases (25.0%), and moderate-positive expression in 2 cases (12.5%). These findings indicate that by the 16–24-hour period, the cellular protective reserves against severe stress may become markedly depleted. In spongiocytes, depletion of lipid inclusions and irreversible cellular alterations were observed, reflecting progressive cellular injury.

According to the pathomorphological findings, the marked reduction or loss of HSP70 expression during the 16–24-hour period may indicate profound exhaustion of the compensatory and protective mechanisms of the adrenal glands under conditions of acute shock induced by birth-related brain injury. This stage may therefore represent a critical phase of irreversible pathological changes associated with severe systemic injury and fatal outcome.

Conclusions. The expression of the HSP70 stress protein in the adrenal cortex of newborns who experienced birth-related brain injury and died within the first 24 hours of life changes markedly and is closely associated with the time interval from birth to death. During the first 0–8 hours of life, the protective response reaches its peak, with high-positive HSP70 expression detected in 87.5% of cases, indicating a pronounced adaptive-compensatory cellular response to acute hypoxia and shock.

During the 8–16-hour period, HSP70 expression decreases substantially due to depletion of intracellular reserves and progression of destructive changes, with low-positive expression observed in 68.75% of cases. This stage may be regarded as a period of subcompensation and progressive attenuation of protective mechanisms, accompanied by the development of irreversible cellular alterations.

During the 16–24-hour period, the stress-protective reserves of adrenal cells become markedly depleted, with negative HSP70 expression observed in 62.5% of cases. This finding indicates profound impairment of the compensatory mechanisms of the adrenal glands under conditions of severe shock and multiorgan dysfunction and reflects progression to a critical stage characterized by irreversible pathological changes associated with fatal outcome.

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