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DIAGNOSIS AND TREATMENT ASPECTS OF SECONDARY NEUROENDOCRINE CHANGES IN ACUTE TWIN BRAIN INJURIES

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Annotation. Nowadays, neuroendocrine symptoms following twin brain injuries (twin brain injuries) are more common and negatively affect the outcome of Brain Double Injuries by reducing the overall quality of life. However, research from the scientific literature suggests that neuroendocrine dysfunctions, particularly hypopituitarism, play an important role in the etiology of complications. It has been found that postoperative hypopituitarism has been a clinically common phenomenon in the last twenty years and is likely to contribute significantly to these disorders, given the parallelism of adenohypophysis among those following neuroendocrine changes associated with hypopituitarism other than cerebral palsy. In this our scientific study, we sought to explore hypothesized pathophysiological mechanisms based on neuroendocrine anomalies after a Brain Double Injury through an overview, improved on the basis of an analysis of early diagnosis and treatment aspects.

Keywords: cerebral palsy, pituitary hormones, brain tissue injuries, clinic, diagnosis, treatment

Currently, neuroendocrine symptoms following traumatic brain injury (TB) are more common and negatively affect the outcome of traumatic brain injury by reducing the overall quality of life. However, research from the scientific literature suggests that neuroendocrine dysfunctions, particularly hypopituitarism, play an important role in the etiology of complications. These cases have been found to be a clinically common phenomenon in the last twenty years of post-traumatic hypopituitarism, and are likely to contribute significantly to these disorders, given the parallelism of adenohypophysis among those following neuroendocrine changes associated with hypopituitarism other than traumatic brain injury. In this our research, we sought to explore hypothesized

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pathophysiological mechanisms based on neuroendocrine anomalies after twin brain injuries through an overview, improved on the basis of an analysis of early diagnosis and treatment aspects.

Brain twin injuries affect approximately 10 million people worldwide each year and 1.7 million in the United States alone (1 - 3). The number of concussions resulting from mild motor trauma and increased use of vehicles in low- and middle-income countries is increasing, which is projected to increase by 50% from 2002 to 2020 (4-6). In addition, sports injuries are also common causes of new brain twin injuries; in fact, in the United States, between 2006 and 2011, nearly 500,000 injuries were reported to the emergency department of sports-related twin brain injuries across the country [7]. In particular, it has been reported that since 2000, more than 300,000 military personnel have been diagnosed with combat brain double injuries (8).

The adenohypophysis above shows the importance of the neuroendocrine secondary changes encountered in the study of brain twin injuries and indicates that the problems have not been fully resolved.

There are also scientific studies that describe a wide range of neurological consequences, from cognitive problems to emotional and behavioral symptoms. Neuropsychiatric complaints play an important role, especially in patients with concomitant brain injuries (9). These include concentration problems, depression, anxiety, fatigue, and loss of emotional well-being, and occur in approximately 30% of patients with brain injury (10 - 16). According to the World Health Organization's International Classification of Diseases, brain injury is defined as the presence of the following three or more symptoms, including headache, dizziness, fatigue, nervousness, insomnia, and decreased concentration, or memory, which should occur within the first month after injury. decrease was observed (18). Long-term consequences such as major depression, alcohol abuse or addiction, panic disorder, or psychotic syndrome have also been reported to be reported after twin brain injuries, regardless of severity (19, 20).

The pituitary gland plays a special role in the study of neuroendocrine secondary changes in brain twin injuries. The pituitary gland sits in a bone called the sphenoid Turkish egarideb, and the membrane is covered by a hard membrane of the brain called the sella. Approximately the size of a pituitary gland, usually weighing less than one gram, it consists of separate sections: the distal part, the tuberal part, and the intermedia part (three of which form the anterior part of the pituitary adenohypophysis), as well as the nervous part (posterior part of the pituitary). The distal part describes the main part of the adenohypophysis, while the tuberalis defines the mask that joins the infundibular stem. The intermedia between the distal part and the neural part is responsible for only a small part of pituitary function. The adenohypophysis produces prolactin primarily through growth hormone (Samatotrp hormone), adrenocorticotropic hormone (Adrenocorticotropic hormone), gonadotropins, thyroid stimulating hormone (Thyrotropic hormone). The posterior pituitary, in contrast, secretes vasopressin and oxytocin from the hypothalamic tract (23).

In our research, the following adenohypophyses were observed in the study of neuroendocrine dysfunctions after double brain injuries.

Pituitary dysfunction is a common complication of twin brain injuries, and has also been found to be observed in the scientific literature. Adenohypophyseal abnormalities in the posterior pituitary gland, such as adrenocorticotropic hormone or insulin-induced growth factor abnormal secretion syndrome, have also been studied in the recognized outcome of double brain injuries, given the clinical manifestations of adenohypophysis fluid balance regulation in the body. In clinical trials. adenohypophyseal abnormalities were observed after head injuries, however, their

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variable clinical manifestations, as well as the subtlety of their symptoms, showed and were difficult to obtain data on these patients.

The first case of traumatic hypopituitarism after double traumatic brain injury was reported in 1918 (24), but until the beginning of this century much attention was paid to this syndromeAdenohypophysis. The literature showed that in a study of 22 patients with mild, moderate, and severe double brain injury due to head injury for at least 3 months (mean 26 months), the authors found that 36.4% of patients had at least one hormonal change in Adenohypophysis. (25) The significant change found was related to the adenohypophysis, with 18.2% of patients not responding adequately to the insulin tolerance test (Instulin tolerance test). As for other hormones, one patient had a impaired corticotrophic response and one had gonadotropin deficiency. (38-40)

Subsequently, in a significantly larger study developed by some authors, 102 patients were examined (27) at least 6 months after injury (19-month average). The authors took more stringent measures to diagnose hypopituitarism by reporting patients with adenohypophyseal insufficiency if they failed both the glucagon stimulation test and the Instulin tolerance test and thus confirmed clinical insufficiency. Despite clear guidelines, adenohypophyseal insufficiency was found in 10.7% of patients and severe growth hormone deficiency was indicated in 8.8%, which was detected in the arginine + adenohypophysis-releasing hormone (GHRH) test. Corticotropic insufficiency was also detected using two provocative tests that provided a 12.7% prevalence of adrenocorticotropic hormone deficiency. In addition, 11.8% of gonadotropin deficiencies were identified, but this was also observed to be age-related.

In our study, prospective studies were performed in 70 patients, assessing pituitary function at 3 and 6 months after injury. Overall, 48% of patients showed at least one adenohypophysis abnormality; After 3 months, insulin-like growth factor 1 (IUUO-1) deficiency was found to be most prevalent in 24% of patients. It has been observed that circulating levels of IGF-1 produced by the liver for adenohypophyseal stimulation may be used to indicate abnormalities in somatotrophic function. It should be noted that low IGF-1 concentrations are specific to UGD; however, its diagnostic sensitivity is low and therefore normal or even high levels cannot exclude growth hormone deficiency. Gonadotropin and cortisol deficiency occurred in 16 and 13.3% of patients, respectively, at the 3-month assessment. It should be noted that these percentages decreased over a 6-month period.

Nevertheless, the results of prospective studies on concomitant short-term and long-term endocrinopathies were found to be very different in terms of predictions, typically ranging from 10 to 58% (38, 45, 46). Therefore, the literature is currently divided on the clinical significance of post-traumatic hypopituitarism, with some claiming that this represents a less diagnosed phenomenon, while others do not occur as often as these proponents suggest (47, 48). Many studies on post-traumatic hypopituitarism have reported the prevalence of pituitary insufficiency due to adenohypophysis, which is a secondary confirmation test. It is also important to recognize that the use of different tests, analyzes, and interruptions has a significant effect on the estimated defect levels (49, 50).

Despite disagreements over the exact prevalence of twin brain injuries, many studies and reviews suggest that hormonal dysfunction, as mentioned above, occurs in some people with brain twin injuries. In fact, the adenohypophysis recommends that they receive pituitary screening within 3–6 months after injury if they have been in the hospital for a long time or show symptoms consistent with pituitary dysfunction (44).

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Interestingly, complaints such as fatigue, depression, anxiety, and emotional well-being also occur in patients with non-secondary chronic neuroendocrine changes in twin brain injuries [51] and have been observed in our patients as well. It is particularly associated with a decline in psychological health, as observed about 30 years ago as a specific clinical syndrome [52]. In research, a decrease in energy and emotional space, social isolation, which leads to greater difficulties with sex, leads to a decrease in quality of life and a greater psychological stress. In addition, growth hormone deficiency after twin brain injuries has been repeatedly demonstrated to be associated with a similar motivation, decreased depression, and a reliable role in trauma adenohypophysis (40, 56 - 58). Therefore, it is not surprising that post-traumatic hypopituitarism and, in particular, post-traumatic brain injury after post-traumatic brain injury have been reconsidered in the context of contusion syndrome, where the same symptoms have previously been considered simply after concussion syndrome. Furthermore, many of the symptoms of post-traumatic stress disorder are associated with concomitant brain injuries, and the question of whether neuroendocrine pathologies can help in conditions of head trauma is answered (59, 60). Although it is very difficult to analyze which symptoms may be related to brain injury, especially those related to brain injury, it is important to know what symptoms may be due to neuroendocrine abnormalities.

A typical neuroendocrine response of the pituitary gland to stress or injury When examining endocrinopathies after a double injury to the brain, it is important to first consider the standard stress effect on the injury to cortisol and other endocrine hormones. In the acute phase of the post-traumatic response (received within the first 24 hours after injury) and subacutely (several days after injury), a predictable neuroendocrine sequence occurs. There is a two-phase model of acute metabolic changes defined as “ebb” and “flow”. First, the sympatadrenal storm occurs within the first few hours after injury, which characterizes the “violence” phase. This involves reducing the overall energy expenditure as the body and brain try to maintain homeostasis by altering normal tissue perfusion. It then enters the “flow” phase, during which catabolic processes provide substrates to repair the damage (63). In general, the acute and subacute periods after injury show a high degree of adenohypophysis function. The adenohypophysis is known to be involved in common signals that contribute to cellular recovery after trauma and enhanced adrenocorticotropic hormone secretion enhances hypercortisolism, metabolic support during treatment, protection against excessive immune responses, and hemodynamic recovery (64, 65).

In our study, until recently, cellular and metabolic events occurring in acute and subacute phases were observed as a long-lasting disease. However, secondary detected changes suggest that the neuroendocrine response to injury changes with prolonged stress (66, 67). Some authors have observed a decrease in adrenocorticotropic hormone, gonadotropic hormone, thyrotropic hormone, and prolactin. The above indicators were also observed in our research.

It is thought that the neuroendocrine and metabolic response in twin brain injuries persists in the same way as in extracerebral injury in the acute and subacute phases (69, 70). For example, the hypopituitarism reported by Van der Berge is said to be caused by a change in the hypothalamus, not the pituitary gland, which differs from its source. In addition, the majority of patients with post-traumatic hypopituitarism have one or more adenohypophyseal abnormalities, but changes occur more extensively in chronic disease.

The mechanisms of neuroendocrine disruption after twin brain injuries were observed as follows.

At present, it remains difficult to study the specific pathophysiological changes that lead to twin brain injuries. However, in addition to reports documenting trauma-related stress-related injuries in the brain (41 - 43), a number of other hypotheses confirmed by experimental data, including adenohypophysis weakness, stem from injury and immune system interference there are also hypotheses.

The pathophysiology of post-traumatic pituitary injury is complex, with primary focal studies leading to secondary injuries due to edema, bleeding, hypotension, and hypoxia (11). Traumatic swelling of the pituitary gland compresses the gland because it sits in a flexible bone compartment and is closed by the adenohypophysis with a diaphragm (44). Fracture forces resulting from trauma can cause direct damage to the pituitary gland itself or to the infundibulum that connects it to the hypothalamus. Fractures of the skull and sella turcica can cause focal damage and have been reported in cases of post-traumatic hypopituitarism (45), but it should be acknowledged that many studies and reports of post-traumatic hypopituitarism have been reported in patients without celiac fracture. Pituitary stem damage can affect pars tuberalisdAdenohypophysis pituitary hormone-producing chromophiles, namely gonadotropin, adrenocorticotropic hormone, and thyroid-producing gonadotropin, corticotropic, and thyrotropic cells (46, 47). The association of post-traumatic hyperprolactinemia with post-traumatic hypopituitarism, as well as secondary pituitary stem compression, leads to the removal of dopaminergic inhibitor control (48). Accordingly, structural damage to the infundibulum can also lead to pituitary insufficiency following twin injuries to the brain by removing hypothalamic access. On the other hand, direct damage to the hypothalamus is not usually considered as a consistent or underlying pathological factor leading to post-traumatic hypopituitarism. However, a recent experiment using a model of intracranial hypertension showed an increase in apoptosis along the HPA axis, such as the hypothalamus, pituitary, and hippocampus (49).

Summarizing the above. Neuropsychiatric symptoms are common in neuroendocrine secondary changes following twin brain injuries. Hypotheses about the pathological roots of these consequences develop for a number of reasons, of which post-traumatic hypopituitarism and, in particular, growth hormone deficiency following post-traumatic brain injury are particularly important. Adenohypophyseal function is common in trauma to brain tissue through pathophysiological pathways such as ischemic injury of the pituitary gland and immune-dependent mechanisms from twin brain injuries, our studies confirm this. As more promising studies are conducted to determine the true prevalence of twin brain injuries, the contribution of these pathophysiological mechanisms to the development of neuropsychiatric symptoms remains to be determined, the accuracy of future efforts. In addition, more modeling for brain tissue injuries is important to uncover the mechanisms of occurrence of double brain injuries, and this will improve the detection and diagnosis of neuroendocrine secondary changes, increase the accuracy of assumptions, and improve patient quality of life.

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