OLGU SUNUMU CASE REPORT

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Dysfunction of Hypothalamic-Pituitary Axis: A Complicating Condition for Rehabilitation in Patients with Traumatic Brain Injury

Hipotalamo-Hipofizer Aks Disfonksiyonu: Travmatik Beyin Hasarlı Hastalarda Rehabilitasyonu Zorlaştıran Bir Durum

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ABSTRACT Traumatic brain injury (TBI) is a leading cause of death and disability worldwide, especially in young adults. While primary injury occurs at the moment of initial biomechanical trauma, secondary injury affecting morbidity, mortality and treatment response occurs in the minutes, hours and days after the primary injury. For centers specialized in early rehabilitation of TBI, it is very important to consider secondary effects of TBI since they have a major role in determining functional abilities of the patients during rehabilitation process. Herein, a case with autonomic and neuro-endocrine dysfunctions secondary to TBI is presented.

Keywords: Traumatic brain injury; hypothalamic-pituitary-axis; hyperhidrosis; rehabilitation

ÖZET Travmatik beyin hasarı (TBH), dünya çapında, özellikle gençlerde, ağır özürlülük ve sıklıkla ölüme yol açabilen bir durumdur. Tüm nörolojik hasar o anda oluşmayıp dakikalar, saatler ve günler sonra da sekonder etkiler ortaya çıkabilir ve bunlar mortalite, morbidite ve tedaviye yanıtları etkileyebilir. Sekonder etkiler, TBH'nin erken rehabilitasyonun uygulandığı merkezler için, rehabilitasyon sırasında hastaların fonksiyonel kazanımları üzerinde etkili olduğu için önemli bir role sahiptir. Burada, TBH'ye sekonder gelişen, otonomik ve endokrin disfonksiyonlu bir olgu sunulmuştur.

Anahtar Kelimeler: Travmatik beyin hasarı; hipotalamo-hipofizer aks; hiperhidrozis; rehabilitasyon

Traumatic brain injury (TBI) is a major cause of death and disability worldwide, especially in young adults. As advanced intensive care facilities available, more patients can survive after severe brain injury, which increases the rates of disability and the risk of socio-economic burden.[1] All neurological damage does not occur at the injury time after TBI, but secondary impact can occur hours and days after the injury and can affect mortality, morbidity and treatment response during rehabilitation process.[2] Secondary injury can cause the autonomic dysfunction, electrolyte imbalance and disturbances of hormonal metabolism leading to systemic dysfunction, which can negatively affect rehabilitation process.[3-5]

Early rehabilitation is an important issue within the context of TBI management. It has been shown that early rehabilitation in the intensive care unit (ICU) has positive effects on the functional prognosis and quality of life of TBI patients.[6] For centers specialized in early rehabilitation of TBI,

it is very important to consider secondary effects of TBI since they have a major role in determining functional abilities of the patients during rehabilitation process.

Here, a case with autonomic and neuro-endocrine dysfunctions as the secondary effects of TBI is presented. These secondary effects of injury affected the rehabilitation process and the case shows the different aspects of the problems complicating the rehabilitation process.

CASE REPORT

Nineteen-year-old woman admitted to the physical medicine and rehabilitation clinic with complaints of the weakness in the left arm and leg, and balance disturbances.

She had a history of TBI following traffic accident three and half months ago. She had been admitted to the emergency room, with Glascow coma scale (GCS) score of 3, and had been intubated. Cranial computerized tomography (CT) revealed multiple fracture lines of the right frontal, occipital and maxillary bones, anterior, posterior, lateral and medial wall of the maxillary sinus and temporoparietal junction, the right frontal, parietal and occipital lobe epidural hematomas with 14 mm at the thickest region, right lateral ventricle compression and 0,5 cm midline shift to the left. The patient was operated for the drainage of hematoma by the neurosurgeons. After surgery, diffusion cranial magnetic resonance imaging (MRI) showed 15 mm and 13 mm bleeding areas causing diffusion restriction at the right frontal lobe, 5 mm thick subdural hematoma filling the right cerebral extra axial field, and restricted diffusion areas consistent with diffuse axonal injury.

Cervical and thoracal vertebral, abdominal and pelvic CT, bilateral vertebral and carotis doppler ultrasonography (USG) were found to be normal. Thorax CT revealed right clavicle fracture and mild contusion regions at the anterior segment of the upper lobe of her right lung. The patient had developed venous thrombotic symptoms including edema, increased temperature and erythema on her left lower extremity at 21st day of the trauma during ICU follow-up. Venous doppler USG demonstrated acute thrombotic changes at the left main femoral vein, saphenofemoral junction, superficial and deep femoral vein. Anticoagulant treatment was started. Beside this anticoagulant treatment the patient was also treated with intravenous metil prednizolon (100 mg/day) and decreased day by day for 10 days and phenytoin at 300 mg/day.

She had been followed in the ICU for two and half months and GCS score increased to 10/15 and she was discharged to home with wheelchair.

On admission to our clinic, she had no distinctive feature in her medical history and neurological examination revealed normal such as levels of consciousness, cooperation and orientation. The only cranial nerve damaged was fascial nerve with central type paralysis. There were disturbances in the body ataxia and in the cerebellar tests.

On physical examination; she was standing with the support of a person, was walking with the support of two caregivers. There was a normal range of motion in the upper and lower extremities. She had a weakness in left upper and lower extremities. She had an upper extremity Brunnstrom stage of 6/6, hand stage of 5/6 and lower extremity stage of 4/6. On sensorial examination two points discrimination in the left was disturbed. Superficial and deep anal sensation and voluntary anal contraction was normal. Deep tendon reflexes were normal in the right but were increased in the left upper and lower extremities. In the assessment of spasticity according to modified Ashworth scale; left hip flexor, adductor and knee flexor muscles were evaluated as 1/4, left foot plantar flexor muscles were evaluated as 2/4.

On systemic examination; she had complaints such as, overeating and weight gaining, hyperhidrosis in the hands, amenorrhea, polyuria without polydipsia, nocturia and nocturnal enuresis. There was edema in left upper and lower extremities. There was a livedoid like appearance in upper and lower extremities, more prominent on the left presented with hyperhidrosis.

The patient was rehabilitated with the program consisting of; cognitive and occupational therapy, balance and coordination exercises, gradual transfer and weight gaining and cold application for spasticity, electrical stimulation for weak muscles, range of movement and stretching exercises for joints and muscles of lower extremities, and strengthening exercises for weak muscles of lower extremities, pelvic floor exercises for complaints such as polyuria, nocturia and nocturnal enuresis because of urodynamic evaluation were normal.

During rehabilitation, as there was an increase in the leg diameter and erythema the process of rehabilitation was stopped and the patient evaluated with doppler USG. Upon detection of partial thrombosis in the left main and superficial femoral vein confirmed the diagnosis of chronic deep vein thrombosis, and the patient was consulted by cardiovascular surgeon. Anticoagulant therapy was started again. Also, there was an increased hyperhidrosis in the patients hands and foot during second therapy (Figures 1, 2: Written and verbal consent was obtained from the patient), the patient was consulted by the dermatology clinic, an aluminum hydroxychloride treatment was started. As the patient had a history of overeating and weight gaining, amenorrhea, polyuria, nocturia and hyperhidrosis, it was thought to be induced by hypothalamo-pituitary axis (HPA) dysfunction, thus, pituitary biochemical parameters were evaluated. Serum prolactin (38.58 (4.79-23.3) ng/mL) and morning cortisol (25.63 (6.2-19.4) ug/dL) levels were high, vasopressin (0.12 (1-5 pg/mL), luteinizing (LH) (0.78 (1-11.4) IU/L) and follicular stimulating hormones (FSH) (1,16 (1.7-7.7) IU/L), and estradiol (25.54 (43.8-211) pg/mL) levels were low. Thyroid stimulating hormone (TSH) (2.69 (0.51-4.30) uIU/mL), adreno corticotropic hormone (ACTH) (41 (0-46) pg/mL), growth hormone (GH) (1.27 (0-8) ng/mL) and somatomedin-c (197.33 (193-575) ng/mL) were found to be normal. The patient was consulted by the endocrinology clinic and follow-up was recommended. Cranial MRI was repeated. Cranial MRI revealed a chronic ischemic changes in the right frontal parietal, occipital lobe and diencephalon. Through these findings, increased cortisol level was considered as secondary effect of the corticosteroid treatment applied after the trauma, and other findings were evaluated as HPA dysfunction secondary to trauma. There was no improvement in hyperhidrosis despite the treatment, eventually botulinum toxin injection as an alternative therapy has not been accepted by the patient. The rehabilitation program was terminated at the end of 3rd month as the patient refused the treatment because of disturbing situation at that moment, and the patient was ambulatory with the ankle-foot orthosis on his left lower extremity under supervision when she was discharged.

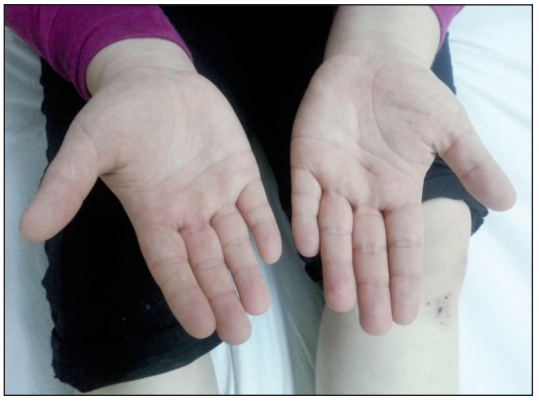

FIGURE 1: View of hyperhidrosis on hands of patients after therapy.

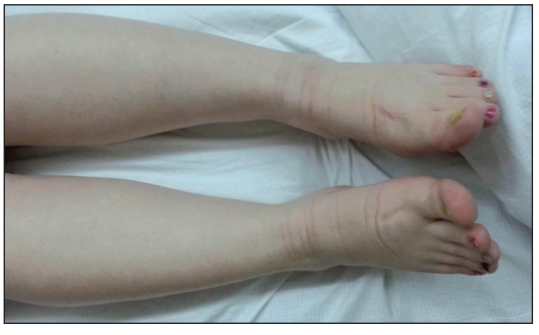

FIGURE 2: View of hyperhidrosis on feet of patients after therapy.

Three months after the discharge, patients menstrual status, polyuria, nocturia, nocturnal enuresis and edematous appearance throughout the body was improved, hyperhidrosis was decreased, and biochemical parameters related to thyroid functional tests, prolactin and cortisol levels were found to be normal.

DISCUSSION

Although the dysfunction of the autonomic and endocrine system in TBI may be caused by direct injury to the HPA, by neuro-endocrinological effects of catecholamine and cytokines, or via systemic infection/inflammation that produces primary gland failure, it has been reported that the secondary traumatic effect is usually the causative factor.[3-5] Compatible to our case study, previous studies have shown that the HPA is usually affected by the presence of hematoma after TBI.[7] Post traumatic brain hemorrhage, edema and a midline shift of midbrain where the hypothalamus is present, may produce a mechanical pressure on the pituitary gland and on the portal system extending from hypothalamus to pituitary gland. This can lead to a disorder in the hypothalamus and pituitary function. In patient with TBI, although the exact mechanism of action is unknown, depending on the hypothalamus injury, the levels of gonadal hormones are more likely to be reduced (up to 80% reduction), as well as 30% reduction in the levels of vasopressin and 15% reduction in thyroid hormone levels.[7] Hyperprolactinemia due to hypothalamic damage has been reported more than half of the patients.[7]

Most common clinical presentation of the HPA disorder is fluid and electrolyte imbalance.[8] Although this situation is usually temporary, persistent cases have also been reported. It has been shown that 3-30 % reduction in vasopressin levels in previous studies and depending on the central diabetes insipidus, as in our case, symptoms such as polyuria, polydipsia and nocturia has been reported.[8]

The anterior hypopituitarism has been reported less often in TBI patients.[9] Generally, hypersecretion of anterior pituitary hormones such as ACTH and prolactin was developing physiologically. Following trauma, activation of the cytokine and noradrenergic system induces the ACTH secretion, which stimulates the secretion of the cortisol from the adrenal gland.[9] Despite the increase in cortisol levels, there is no suppression of ACTH as feedback mechanisms are disrupted. Exogenous corticosteroid intake can cause suppression of ACTH. In our case, despite normal levels of ACTH, the increase in cortisol levels may be explained by dexamethasone treatment administered to the patient during early posttraumatic period, moreover it can be concluded that the ACTH elevation may be masked in relation to exogenous cortisol. The increased appetite, weight gain, edema and increase in the tendency to venous thrombosis are considered to be linked with the increase in cortisol levels.

The other pituitary hormones such as GH and TSH levels were within the normal limits, the FSH, LH and estradiol levels were low.

In a previous study carried out during the early period following moderate to severe TBI, pituitary hormones showed 3.8% decrease in TSH levels, 40% decrease in gonadotrophin levels, 8.8% decrease in ACTH and 20% decrease in GH levels have been reported.[10] In a study of similar patients with an average 12 days following TBI, 2% decrease in TSH, %80 decrease in gonadotrophins, 16% decrease in ACTH and %18 decrease in GH levels have been reported.[11] In the light of these studies, it can be proposed that the early normalization in the levels of TSH, ACTH and GH after trauma may be related to compensatory mechanisms linked to recovery, and the more marked decrease in the levels of gonadotrophin can be seen. Hormone levels were measured 3.5 months after the trauma in our case. During the intervening time, the compensatory mechanisms might have returned the GH and TSH levels toward to normal. In terms of gonadotropin, as reported in previous studies, due to more serious interactions or due to already existing negative effects of hyperprolactinemia, FSH, LH and estradiol levels might be detected low. In concordance with our assumption, in a meta-analysis, it has been reported that 30% of the prolactin elevation continued in TBI patients in the chronic phase.[7]

In our case, the most significant symptom affecting rehabilitation process was increased palmoplantar hyperhidrosis. Hyperhidrosis can occur due to many reasons such as, infections, drugs, malignancies, and neurologic, metabolic and endocrine disturbances.[12] TBI can cause damage to the connection between the hypothalamus and the cortex

which would induce the autonomic hyperactivity. It has been reported that, this situation can arise from a lesion at the central inhibitory pathway which prevents the occurence of excessive autonomic responses and regulates afferent stimuli.[12] Our patient also had a history of diffuse brain injury occurring over a wide area.

In conclusion, TBI has been shown to be one of the most common causes of the hypothalamus and pituitary dysfunction. In parallel with trauma healing process, there may be a partial or complete recovery of this dysfunction, but it can affect the patient's rehabilitation process, and negatively affects the continuity of care.

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