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Central Diabetes Insipidus in a Quadriplegic Patient without Direct Trauma to the Head: A Rare Complication

Kafa Travması Eşlik Etmeyen Kuadriplejik Bir Hastada Santral Diabetes İnsipidus: Nadir Bir Komplikasyon

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ABSTRACT This report highlights the clinical significance of central diabetes insipidus (CDI), a rare complication that arises following acute traumatic cervical spinal cord injury without head injury. The aim was to emphasize the importance of considering CDI during the rehabilitation process. A 25-year-old male patient diagnosed with a C4 level (ASIA A). No head trauma was detected in the patient's examinations. The patient reported symptoms of dry mouth, excessive thirst, and increased water intake during the neurosurgery clinic evaluation. The patient was diagnosed with CDI. During hospitalization, the patient's fluid intake ranged from 3,000 to 4,000 mL daily. With a strict fluid regimen and urine monitoring, the patient's laboratory findings improved within 2 weeks. Being aware of the potential symptoms of diabetes insipidus that may accompany spinal cord injuries enables the rapid implementation of appropriate treatment and fluid management strategies. This helps maintain the patients' overall health and minimizes potential complications.

Keywords: Quadriplegia; head trauma; spinal cord injury; diabetes insipidus

ÖZET Bu vaka, kafa travması olmaksızın akut travmatik servikal omurilik yaralanmasını takiben ortaya çıkan nadir bir komplikasyon olan santral diabetes insipidusun (SDİ) klinik önemini vurgulamaktadır. Bu çalışmanın amacı, rehabilitasyon sürecinde SDİ'nin göz önünde bulundurulmasının önemini vurgulamaktır. Yirmi beş yaşındaki erkek hasta C4 ASIA A tanısı ile takip ediliyordu. Hastanın değerlendirmelerinde kafa travmasının eşlik etmediği saptandı. Hastanın takiplerinde, ağız kuruluğu, aşırı susama ve artmış su tüketimi şikâyetleri gelişmiştir. Hastaya SDİ tanısı konulmuştur. Hastanede yatış süresince hastanın günlük sıvı alımı 3.000-4.000 mL arasında değişmiştir. Sıkı bir sıvı rejimi ve idrar takibi ile hastanın laboratuvar bulguları 2 hafta içinde düzelmiştir. Omurilik yaralanmalarına eşlik edebilecek diabetes inspidus semptomlarının farkında olunması, uygun tedavi ve sıvı yönetim stratejilerinin hızla uygulanmasını sağlar. Bu durum, hastaların genel sağlığının korunmasına yardımcı olur ve potansiyel komplikasyonları en aza indirir.

Anahtar Kelimeler: Kuadripleji; kafa travması; spinal kord hasarı; diabetes inspidus

Spinal cord injuries (SCI) typically result in sensory, motor, and autonomic deficits below the level of the lesion.[1] SCI is a traumatic event with limited recovery of function despite the best efforts of many researchers to devise realistic therapeutic treatments. SCI primarily affects young adults, with nearly half of all injuries occurring between the ages of 16 and 30. The average age at injury has increased from 29 years during the 1970s to 43 years since 2015.[2,3]

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The National Spinal Cord Injury Statistics Center data estimated that the annual SCI incidence is approximately 54 cases per million people, or 17,810 new cases each year in the U.S.[2]

Published data on the epidemiology of SCI in Türkiye are limited to a few studies. Karacan et al. reported an epidemiological study conducted by 49 provinces, and accordingly stated that the annual SCI incidence is 12.7 cases per million people.[4]

Since 2015, motor vehicle crashes have taken the first place of reported SCI cases (38.6%).The most common causes include falls (32.2%), followed by acts of violence (primarily gunshot wounds, 14%) and recreational sports activities (7.8%).[2] Violence caused 13.3% of SCI prior to 1980, and peaked between 1990 and 1999 at 24.8% before declining to only 14.3% since 2010.[3] In Türkiye, the most common cause of injury is motor vehicle accidents (48.8%), followed by falls (36.5%), stab wounds (3.3%), violence (1.9%), and injuries after diving (1.2%).[4]

The most common levels of SCI injury were C5 and C6 among tetraplegic and T12 and L1 among paraplegics. C5 is the most common vertebral damage level, followed by C4, C6, T12, and L1 levels.5 Recently, incomplete tetraplegia was the most frequent neurological category at discharge of persons reported in the database (47.2%), followed by incomplete paraplegia (19.6%), complete paraplegia (20.2%), and complete tetraplegia (12.3%). Less than 1% of the patients experienced complete neurological recovery by the time of hospital discharge.[2,5]

Secondary complications were present during both the acute care units and inpatient rehabilitation services. These include pulmonary, cardiovascular, and gastrointestinal complications, bladder and bowel problems, spasticity, pressure ulcers, neuropathic pain, syringomyelia, osteoporosis, autonomic dysreflexia, and upper extremity overuse syndromes. The presence of secondary complications may decrease the health-related quality of life, limit function recovery, and increase the morbidity and mortality rates.[6]

Diabetes insipidus is a rare disorder of water homeostasis characterized by excreting excessive volumes of hypotonic urine (polyuria). Over 90% of the vasopressinergic neurons that project from the supraoptic and paraventricular nuclei to terminate in the posterior pituitary must be destroyed in order to cause vasopressin (AVP) deficiency sufficient to lead to polyuric symptoms. Central diabetes insipidus (CDI) is the clinical manifestation of the destruction of the neurons of the hypothalamus/posterior pituitary axis, with consequent loss of AVP secretion. In many patients, CDI is caused by the destruction or degeneration of neurons originating in the supraoptic and paraventricular nuclei. It is clinically characterized by polydipsia and polyuria (urine output >30 mL/kg/day) of dilute urine (<250 mOsm/L).[7]

Diabetes insipidus arises from one of several causes and can be classified as either primary or secondary.[8] The primary causes are either idiopathic or familial. The secondary group consists mainly of local inflammatory or autoimmune diseases, craniocerebral traumas, Langerhans cell histiocytosis, infections, neoplastic diseases, trauma resulting from surgery or an accident (e.g SCI), metastases, and midline cerebral and cranial malformations.[9-11] In the presence of polyuria and polydipsia symptoms developing during the follow-up of patients with spinal cord injury, the diagnosis of CDI should not be overlooked.[12,13]

We present a case of CDI that developed after a gunshot injury to the cervical spinal cord unassociated with a head injury. We aimed to discuss the disease process in light of the relevant literature and to emphasize restoring and compensating for the loss of functioning and preventing or slowing deterioration in functioning in every area of a person's life during the rehabilitation process.

CASE REPORT

A 25-year-old male patient presented to the emergency department following a gunshot wound to his posterior neck region. The computer tomography (CT) taken in the emergency room revealed that the bullet core was placed in the cervical (C5) vertebra corpus and caused a fracture in the left lamina of the C6 vertebra. In cervical spinal magnetic resonance imaging (MRI), heterogeneous signal changes were

observed in the posterior elements at the level of the C5-C6 vertebrae, and heterogeneous signal changes were detected in an area of approximately 13x24 mm in the cervical spinal cord at this level. No mass lesion that could be differentiated from the brain parenchyma was detected in brain CT. The cerebral parenchyma, posterior fossa, and cerebral sulcus were normal, and the ventricles were symmetrical and in normal calibration. In addition, the midline structures were in place and no lytic-destructive lesions were observed in the bone structures. Radiographs of the thoracic spine showed no vertebral abnormalities. The abdominal CT revealed no acute pathology. The patient was operated by the neurosurgery clinic, and the bullet in the C5 vertebra was removed, and unilateral laminectomy was performed in the left C6 vertebra. The patient is not indicated for a vertebral stabilization operation.

The patient, who was taken to the physical therapy and rehabilitation program in the early postoperative period, was transferred to our hospital for an advanced rehabilitation program in the fourth week after his medical condition stabilized. At the initial physical examination, the general condition of the patient was good, he was conscious, and his cooperation and orientation were complete. The bilateral shoulder elevation muscle strength were 5/5, shoulder abduction 2/2, elbow flexion (C5) 3/1+,wrist extensors (C6) and other distal muscles were 0/5 based on the Global Oxford Scale. The deep tendon reflexes of the upper and lower extremities were hypoactive. On sensory examinations; C5 and distal dermatomes were anesthetic. The pathological reflexes were negative. No sensory or motor functions are preserved in the sacral segments S4-5. The patient was at the in-bed level and there was no support/unsupported sitting balance. The patient's neurological examinations were determined to be C4 ASIA A with sensory and motor examination without deep anal pressure sensation and internal anal sphincter contraction.

In the history of the patient has been learned, he complained of dry mouth, drink too much water and excessive thirst on the neurosurgery clinic. After the endocrine and psychiatric consultations and examinations requested for differential diagnosis, the patient was diagnosed with central diabetes insipitus and orally initiated desmopressin acetate 120 mcg/day.

The early period of his rehabilitation program included passive range of motion exercises for the lower and upper extremities twice a day, progressive resistive and active assistive exercises to increase existing muscle strength, breathing exercises, vascular endurance program on the gradual tilt table, and mobilization programs to increase trunk balance. During the follow-up of the patient, occasional hypotension attacks were detected. The hemodynamic status of the patient was followed closely.

During the hospitalization follow-up, it was observed that the daily fluid intake was around 3,000-4,000 mL, and the urine output varied between 6,400 and 7,400 mL and continued at a very high level. Laboratory examinations of the patient after the introduction and drug regulation are given in Table 1. Blood pressure values were found to be within normal limits. The desmopressin acetate dose of the patient was gradually increased up to 240 mcg/day in consultation with the internal medicine and nephrology department during the decision-making phase in terms of monitoring the patient's current polyuria and fluid deficit. We monitored the patient's urea and electrolytes regularly for evidence of dehydration, renal hypoperfusion, or electrolyte imbalance. Laboratory findings improved after 2 weeks of strict fluid regimen and urine follow-up. It was decided to continue the desmopressin acetate dose as 240 mcg/day. At follow-up, all his laboratory parameters were nor-

TABLE 1: Laboratory results before and after treatment.

	Before treatment	After treatment
Serum sodium (mEq/L)	134	138
GFR (mL/minute/1.73 m^2)	162	145
Creatinin (mg/dL)	0.42	0.55
Chloride (mmol/L)	100	103
Ca (mg/dL)	9.9	9.5
Urine specific gravity (N.1020-1028)	1.010	1020-1030
Urine osmolality (mOsm/L)	143	184
Serum osmolality (mOsm/L)	284	285
Daily urine output	6400-7400	2250-3000

GFR: Glomerular filtration rate; Ca: Calcium.

mal. Our patient was still using a dose of 240 mcg/day in the follow-up at the 3rd month. The participant provided written informed consent.

DISCUSSION

Head injury and SCI are common occurrences in neuro-surgical practice. They account for an important proportion of care, reduce disability, and ethical issues. The reported incidence of cervical spine trauma after clinically significant head injury generally ranges from 4% to 8%.[14] Hypercalcemia is common in children (24%) and young adults after SCI. Hypercalciuria develops within the first week after injury and can last for 6 months or longer. Symptoms typically present 4-8 weeks after SCI. Symptoms include anorexia, nausea, lethargy, polydipsia, and polyuria. As early as 3 months, the bones become osteoporotic and long bone fractures can be seen. It has been shown that parathyroid hormone and vitamin D levels are significantly suppressed in patients after SCI. It has been reported that this suppression returns to normal within six months.[14] As the patient's blood calcium levels, as well as vitamin D levels, were within normal ranges upon admission, it was concluded that the patient's symptoms were unlikely to be attributable to hypercalcemia.

Berezin et al. reported that six women with a traumatic SCI developed hyperprolactinemia, amenorrhea, and galactorrhea. Five of them had thoracic level lesions and 1 had a lumbosacral lesion. A case developed transient diabetes insipidus. The authors hypothesize that one or more of the following factors might play a role in the pathogenesis of this syndrome: pituitary stalk concussion or concussion, the elevated level of endorphins lasted only for the duration of the spinal shock, or injury of the afferent neuronal pathway of the spinal cord.[15]

The initial mechanical in acute SCI forces delivered to the spinal cord at the time of injury is known as primary injury where "displaced bone fragments, disc materials, and/or ligaments bruise or tear into the spinal cord tissue".[16] Four main characteristic mechanisms of primary injury have been identified that include: (1) Impact plus persistent compression; (2) Impact alone with transient compression; (3) Distraction; (4) Laceration/transection.[17] Damage in this process is irreversible.

Secondary injury can be temporally divided into acute, sub-acute, and chronic phases. The acute phase begins immediately following SCI and includes vascular damage, ionic imbalance, neurotransmitter accumulation (excitotoxicity), free radical formation, calcium influx, lipid peroxidation, inflammation, edema, and necrotic cell apopythosis. As the injury progresses, the sub-acute phase of the injury begins, which involves apoptosis, demyelination of surviving axons, Wallerian degeneration, axonal dieback, matrix remodeling, and evolution of a glial scar around the injury site. Further changes occur in the chronic phase of injury, including the formation of a cystic cavity, progressive axonal die-back, and maturation of the glial scar.[18-20]

In addition to direct tissue damage due to gunshot wound injuries, permanent tissue damage such as ischemia, thrombosis, and necrosis should be considered due to thermal effects as well as the direct impact of the bullet, the pressure of shock waves and the temporary cavitation effect in surrounding tissues, especially in neural structures. Three mechanisms of tissue damage: the direct impact of the bullet, the pressure of shock waves and the temporary cavitation after gunshot wound injuries.[21] Mirovsky et al. verified that the cause of neurologic deficit in patients following gunshot wounds is direct trauma to the spinal cord by the bullet, bone fragments, or in rare cases by disc fragments compressing the cord.[22]

Some of the underlying causes of CDI are iatrogenic post-neurosurgery (20%), head trauma (16%) and inherited/familial (1%).16 Postraumatic CDI can be caused by any type of head trauma; however, it most commonly occurs secondary to road traffic accidents.[23] Trauma can cause anterior pituitary dysfunction or CDI and often occurs in patients with associated skull fractures or neurological defects.[24,25] In some cases (6%) no CT/MRI finding is demonstrated, and hypoxic damage or diffuse axonal injury is presumed to be the cause.[26]

Machiedo et al. reported the development of CDI in three cases following non-cranial trauma. They associated the etiology of CDI in patients, the

mechanism that best explains the syndrome is shock from hypovolemia with occlusion of vessels resulting in tissue hypoxia and necrosis.[27]

Hypotension is commonly observed during the spinal shock phase following a spinal cord injury, primarily due to reduced sympathetic tone and vasodilation. CDI can rarely occur in adults without trauma due to hypoxemia and hypoperfusion.[28]

Traumatic SCI in all spine segments occurs in 5%-15% of patients with severe head injury and may be accompanied by head trauma complications. Although an increasing injury severity has been associated, as measured by the Glasgow Coma Scale, 7 severe and moderate head injury may cause misdiagnosis of SCI, leading to devastating long-term consequences.[29,30] Should be alert to the possibility of diabetes inspidus that may develop after SCI and fluid management is a critical aspect of SCI patient care, especially in the following CDI inpatient medical setting. Fluid management is important in these patients and must be careful consideration of their individual fluid needs.

Especially in acute rehabilitation clinics, the possibility of CDI should be kept in mind by taking into account the symptoms such as polydipsia and polyuria and by performing strict and careful fluid intake and urine discharge follow-ups along with routine laboratory analyses. Therefore, mortality can be prevented by the early diagnosis and treatment of life-threatening complications such as CDI.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Sefa Gümrük Aslan;* ***Design:*** *Sefa Gümrük Aslan;* ***Data Collection and/or Processing:*** *Sefa Gümrük Aslan, Esra Ülgen Kıratlıoğlu;* ***Analysis and/or Interpretation:*** *Sefa Gümrük Aslan, Esra Ülgen Kıratlıoğlu, Kutay Tezel;* ***Literature Review:*** *Sefa Gümrük Aslan, Esra Ülgen Kıratlıoğlu, Kutay Tezel;* ***Critical Review:*** *Nilüfer Kutay Ordu Gökkaya.*

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