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Neuroendocrine Abnormalities in Traumatic Brain Injury

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ABSTRACT:
Traumatic brain injury happens when the head hits on something violently or when the head hits repeatedly, or when an object enters through the skull and into the brain. TBI can cause hormone problems. A person with TBI may have hormone problems soon after the hit or months or even years after the injury. The two main parts of the endocrine system are the pituitary gland and the hypothalamus, located inside or near the brain. TBI can injure them and causes hormone problems. This is a case series thathighlights the importance of being aware of endocrine sequelae even decades after serious TBI.
Keywords: Traumatic brain injury, Adrenal insufficiency, Diabetes insipidus,Cerebral salt wasting syndrome, SIADH

I. INTRODUCTION:

Neuroendocrine manifestation in Traumatic brain injury can deteriorate consciousness and may even lead to death. In the last two decades, traumatic brain injury (TBI) as a major and perhaps formerly underestimated cause of hypothalamic-pituitary dysfunction has been intensely researched and discussed in the medical literature. In this case series, we discuss in detail about neuroendocrine abnormality in TBI.

1)Case report:

The case is of a 28-year-old male patient who presented to the emergency department with c/o with lethargy, weakness, anorexia, nausea & vomiting, and weight loss. He is a case of Traumatic brain injury sequelae, now referred for neurorehabilitation in the department ofPhysicalMedicine and Rehabilitation. There was no history of any other disease in the past.

On examination, he is poorly built and nourished, dehydrated, loss of pubic, facial, and axillary hair,muscular atrophy Vitals BP- 100/60 mmhg, PR- 98 beats/minute sinus rhythm, normal volume character, and condition of the vessel wall, oxygen saturation-94%, respiratory rate – 20 cycles/ mi. abdominal tenderness was present. Blood investigations showed: sugar 70 mg/dl, serum sodium- 122 mmol/l (135.0 - 148.0 (mmol/l), serum potassium- 5.8 mmol/l (3.5 - 5.1 mmol/l), urine spot sodium- 35, 9 am serum cortisol- 0.9 µg/dL (2.3 – 19.4µg/dL), ACTH-0.9pmol/L (1.5-14.7), Total testosterone-14.5 nmol/L (9.9–27.8), Sex hormone binding globulin-45.5 nmol/L (15-48), Luteinizing hormone-3.2mU/L (1.7-8.6), Follicle stimulating hormone-4.2 mU/L (1.5-12.4), Prolactin-89mU/L (86-324) TSH-4 uIU/mL (0.27 – 4.2 uIU/mL), IGF-1 14 nmol/L (12.2-32.8) and other investigation are within normal in limits. MRI brain was taken, it showed a flattened pituitary gland at the bottom of the sella and the tissue adjacent to the right cavernous sinus compatible with dislocated pituitary tissue after fracture of the middle cranial fossa. The patient was treated with IV fluids, dextrose, and IV hydrocortisone sixth hourly for the first day. Oral replacement started after 24 hours and be reduced to maintenance over 3-4 days.

2) Case report:

54-year-old male with no comorbidity has admitted under physical medicine andrehabilitationafter traumatic brain injury now c/o fatigue, weakness, dizziness whilestanding and increasedthirst. Patient's urine output was more than 3L/day. On examination vitalsPR- 82 bpm, BP onlying down – 130/80 mmhg, on standing 100/60mmhg, oxygen saturation-94%,respiratory rate – 20 cycles, Skin pinch – going back slowly. Blood investigation FBS-90mg/dl, PPBS -120 mg/dl,HbA1c-5.8% (<6.5%)S. sodium- 149 mmol/l (135.0 - 148.0 mmol/l),S.potassium- 4.1 mmol/l (3.5 - 5.1 mmol/l), urea–28 mg/dl (8.0-49 mg/dl), S. creatinine – 07mg/dl (0.7-1.2 mg/dl), TSH-1.66 uIU/mL (0.27-4.2 uIU/mL), Serum osmolality – 310mOsm/kg (285-290 mOsm/kg), Early morning urine osmolality- 154mOsm/kg (300-900 mOsm/kg), We couldnot do the water deprivation test because of hypernatremia. Serum AVP – 0.56pg/ml (>1 pg/ml).We have started him on intra nasal DDAVP 10 mcgatnight. After one week, there was no posturalhypotension,Early morning urine osmolality- 640mOsm/kg (300-900 mOsm/kg), serum sodium140mmol/l (135.0 - 148.0 mmol/l). Patient was symptomatically better.

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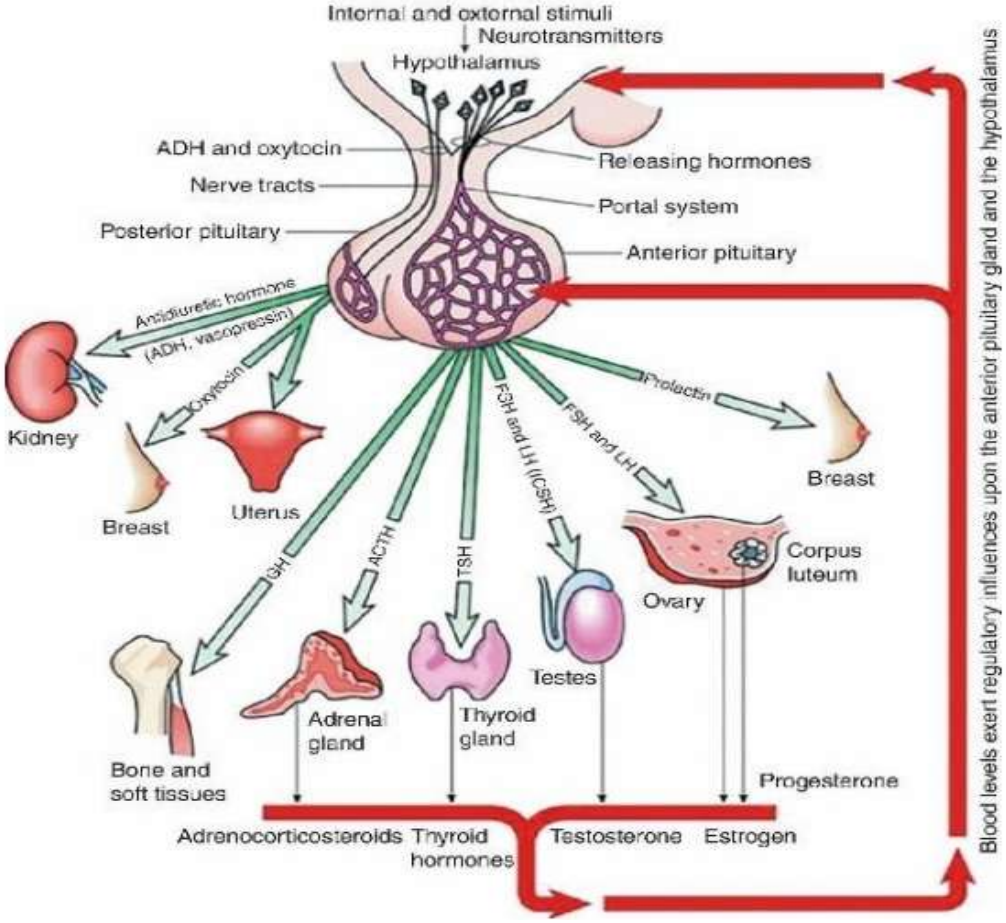
II. DISCUSSION:

The central neuroendocrine system is made up of the hypothalamus and the anterior and posterior lobes of the pituitary gland. The hypothalamus is a section of the forebrain below the thalamus that coordinates the interactions of the neuroendocrine system.The pituitary gland (hypophysis) sits in the sella turcica, which is a bony cavity within the sphenoid bone and is connected to the hypothalamus by the pituitary stalk. The larger anterior lobe of the pituitary (adenohypophysis) stores and releases a number of hormones under the influence of the hypothalamus, including follicle-stimulating hormone (FSH), luteinizing hormone (LH), adrenocorticotropic hormone (ACTH), thyroidstimulating hormone (TSH), prolactin, and growth hormone (GH). The smaller posterior lobe of the pituitary (neurohypophysis) is responsible for the storage and release of oxytocin and antidiuretic hormone (ADH), also known as vasopressin. These hormones are produced by the hypothalamus and then travel to the posterior pituitary via the pituitary stalk, where they are eventually released. This makes these two hormones especially susceptible to neuronal damage at the level of the hypothalamus and stalk, as well as the pituitary gland itself.



Adrenal insufficiency

When the adrenal glands don't make enough hormones; results in anorexia, nausea, vomiting, fatigue, postural dizziness, abdominal pain, limb and back pain, and impaired consciousness. Shared biochemical perturbations include hyponatremia, hyperkalemia (in primary adrenal insufficiency [Addison's disease and congenital adrenal hyperplasia]), and hypoglycemia (more common in children than in adults). Hyponatremia is a characteristic biochemical feature in primary adrenal insufficiency and is found in 80% of patients at presentation. Hyperkalemia is present in 40% of patients at initial diagnosis. Hyponatremia is primarily caused by mineralocorticoid deficiency but can also occur in secondary adrenal insufficiency due to diminished inhibition of antidiuretic hormone (ADH) release by cortisol, resulting in mild syndrome of inappropriate secretion of antidiuretic hormone (SIADH).

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Cortisol has a circulating half-life of 90 minutes; hence, tissues become deficient within several hours after cortisol deprivation. Cortisol has highly pleiotropic effects that are due to transcriptional modulation of genes bearing a glucocorticoid response element (29% of all genes). The physiological consequences of cortisol deficiency are extensive and start with loss of the normal suppressive action of endogenous glucocorticoids on inflammatory cytokines, resulting in rapid increases in cytokine levels, which cause fever, malaise, anorexia, and bodily pain. Consequently, cortisol deficiency leads to altered immune-cell populations (neutropenia, eosinophilia, and lymphocytosis); loss of the synergistic action of cortisol with catecholamines on vascular reactivity, leading to vasodilatation and hypotension; hepatic effects on intermediary metabolism, with reduced gluconeogenesis, hypoglycemia, or both; and reduced circulating free fatty acids and amino acids.

At the cellular level, loss of cortisol depresses the action of activator protein 1 (AP-1) and nuclear factor κB (NF-κB), leading to the unfettered activation of genes that produce inflammatory proteins, since the normal cortisol inhibition of the binding of NF-κB to the glucocorticoid receptor is lost.

The diagnosis of adrenal insufficiency is established by the short cosyntropin test, a safe and reliable tool with excellent predictive diagnostic value. The cut-off for failure is usually defined at cortisol levels of <450–500 nmol/L (16–18 μg/dL) sampled 30–60 min after ACTH stimulation. During the early phase of HPA disruption (e.g., within 4 weeks of pituitary insufficiency), patients may still respond to exogenous ACTH stimulation. In this circumstance, the ITT is an alternative choice but is more invasive and should be carried out only under a specialist's supervision.

Glucocorticoid replacement for the treatment of chronic adrenal insufficiency should be administered at a dose that replaces the physiologic daily cortisol production, which is usuallyachieved by the oral administration of 15–25 mg hydrocortisone in two to three divided doses.

Diabetes insipidus

Hypernatremia following acute TBI warrants a workup to rule out diabetes insipidus (DI). There are two types, pituitary/central and nephrogenic. Pituitary or central DI is associated with TBI and it is believed to occur from injury to the neurohypophysis. Oftentimes, it is associated with skull fractures near the sella turcica, which may tear the stalk of the pituitary gland, disrupting ADH secretion from the posterior pituitary gland. With low levels of ADH, there is excessive volume depletion from renal water loss, leading to hypernatremia and plasma hyperosmolarity. Patients will typically present with signs of dehydration due to passing high volumes of dilute urine, including excessive thirst and polydipsia. Laboratory workup includes a 24-hour urine collection for determination of urine volume and urinary specific gravity, which is typically less than 1.005 in patients with DI. Serum and urine studies reveal a high serum sodium (>145 mEq/L) and high serum osmolality (>280 mOsm/kg) combined with a low urine osmolality. The drug of choice for treatment of DI is desmopressin acetate (DDAVP), which is an analog of ADH that has a prolonged antidiuretic effect. DDAVP is available in subcutaneous, intravenous, intranasal, and oral preparations.

SIADH

One of the most common neuroendocrine disorders encountered in TBI patients is the syndrome of inappropriate antidiuretic hormone secretion (SIADH). This syndrome is suspected in the setting of hyponatremia, which requires investigation to differentiate from other causes of low serum sodium.The criteria for diagnosing SIADH include hyponatremia with corresponding serum hypoosmolality, continued renal excretion of Na +, urine less than maximally dilute, absence of clinical evidence of volume depletion (normal skin turgor, blood pressure within the reference range),absence of other causes of hyponatremia (adrenal insufficiency, hypothyroidism, cardiac failure, pituitary insufficiency, renal disease with salt wastage, hepatic disease, drugs that impair renal water excretion), and correction of hyponatremia by fluid restriction. Head trauma can disrupt posterior pituitary function and is among the reasons why ADH is secreted at inappropriate levels despite plasma hypo-osmolality and normal or increased plasma volume. A mainstay of treatment in most cases is fluid restriction to about 1.0 to 1.2 L per 24 hours with daily serum sodium monitoring. Strictly monitoring fluid inputs and outputs helps to ensure fluid intake is less than the combined loss through urine output and insensible loss.

Cerebral salt wasting syndrome

This is characterized by extracellular volume depletion caused by a renal sodium transport abnormality in patients with intracranial disease and normal adrenal and thyroid function.

CSW typically occurs in the setting of acute CNS disease or trauma. Conditions leading to cerebral salt-wasting syndrome include head injury, brain tumor, intracranial surgery, stroke, intracerebral hemorrhage, tuberculous meningitis, and craniosynostosis repair. However, CSW can also occur in the absence of cerebral disease. Hyponatremia in CSW will present with some similar signs and symptoms described in SIADH, including lethargy, agitation, headache, altered consciousness, seizures, and coma. Similarly, the severity of symptoms typically reflects the magnitude and rapidity of the decrease in serum sodium concentration. The differentiation of SIADH from CSW depends on an accurate estimation of extracellular volume. Unfortunately, no single physical finding can accurately and reproducibly measure this volume. Therefore, indirect signs of hypovolemia should be investigated, including orthostatic hypotension, increased capillary refill time, decreased skin turgor, dry mucous membranes, and a sunken anterior fontanel. These signs usually appear only when the degree of dehydration is moderate to severe. Similar to SIADH, the laboratory finding in CSW includes elevated urinary sodium concentrations and low serum osmolality. The main differentiating factor between the two conditions is the extracellular fluid volume, which is low in CSW. Management of CSW syndrome centers on correction of intravascular volume depletion and hyponatremia, as well as on replacement of ongoing urinary sodium loss, usually with intravenous (IV) hypertonic saline solutions. It is of utmost importance to distinguish CSW syndrome from SIADH because improper treatment (i.e., fluid restriction) may lead to worsening intravascular volume depletion, which would potentially jeopardize cerebral perfusion by lowering system blood pressure.

Hypothyroidism**:**Fatigue, constipation, weight gain, irregular menstrual periods, cold intolerance

Hypogonadism**:**In women, a stop in menstruation and loss of body hair; in men, sexual dysfunction, breast enlargement, loss of body hair, and muscle loss.

Growth hormone deficiency**:**In adults, increased fat, loss of muscle and bone, and decreased energy; in kids, growth problems.

Hyperprolactinemia**:**Irregular menstrual periods, nipple discharge, and erectile dysfunction.

III. CONCLUSION:

Thecaseseries of hyponatremia in TBI is chosen because this can lead to a rapid deterioration of consciousness and even may lead to seizure, coma and death. Evidence also suggested that hypopituitarism is greater in persons with severe compared with those with mild or moderate TBI. Clinicians must be aware that TBI can cause neuroendocrine manifestation

REFERENCE

[1]. Delisa's physical medicine and rehabilitation 6th edition, Chapter 19.
[2]. N Engl J Med 2019; 381:852-861DOI: 10.1056/NEJMra1807486.
[3]. Harrison Manual of Medicine 20th Edition, Chapter 379
[4]. Delisa's physical medicine and rehabilitation 6th edition Chapter 6
[5]. The Journal of Clinical Endocrinology & Metabolism, Volume 98, Issue 3, 1 March 2013, Pages 27A–28A