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Review Article

Report of a Very Rare Syndrome Abnormal and Inappropriate Secretion of Antidiuretic Hormone from the Posterior Pituitary Due to Occipital Bone Fracture

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Abstract

A 70-year-old man suffered an occipital bone fracture due to feint and was discharged from the central hospital for recovery after ten days in the neurosurgery department and was monitored in a local hospital. After 48 hours without any provocative or unexpected factors, the patient developed delirium, extreme lethargy, and finally became semi-comatose. He was sent back to the hospital and was monitored in the intensive care unit. Since no new reasons were found for the occurrence of symptoms, he was transferred to the endocrinology department, where he was diagnosed with syndrome of excessive secretion of antidiuretic hormone due to trauma to the posterior pituitary gland.

Introduction

Antidiuretic hormone (ADH) is produced by a region of the brain called the hypothalamus. This hormone is stored and released in the pituitary gland. ADH controls how the body releases and stores water. When ADH (also called vasopressin) is produced in excess, the condition is called syndrome of inappropriate antidiuretic hormone secretion (SIADH). This overproduction can occur in places other than the hypothalamus.

Syndrome of inappropriate ADH secretion (SIADH) is a condition defined by uncontrolled secretion of antidiuretic hormone (ADH) from the pituitary gland or non-pituitary sources or by its continued action on vasopressin receptors. The condition was first diagnosed in 1967 in two patients with lung cancer by William Schwartz and Frederick Barter. They developed the classic Schwartz and Barter criteria for diagnosing SIADH, which have not changed to this day. SIADH is characterized by impaired water excretion resulting in hyponatremia with hypervolemia or euvolemia.

Physiology:

Normal Physiology

A. Antidiuretic hormone (ADH) (also known as vasopressin) is produced by the hypothalamus in response to increased serum osmolality.
B. ADH is transported from the hypothalamus to the posterior pituitary gland.
C. ADH is released into the circulation by the posterior pituitary gland.
D. ADH then travels to the kidneys, where it binds to ADH receptors on the distal convoluted tubules.
E. Binding of ADH to these receptors causes aquaporin-2 channels to move from the cytoplasm to the apical membrane of the tubules. These aquaporin-2 channels allow water to be reabsorbed from the

collecting ducts and returned to the bloodstream. This results in a decrease in the volume and increase in the osmolality (concentration) of the urine excreted.

F. The excess water that is reabsorbed reenters the circulation, reducing serum osmolality.

G. This decrease in serum osmolality is sensed by the hypothalamus and results in a decrease in ADH production.

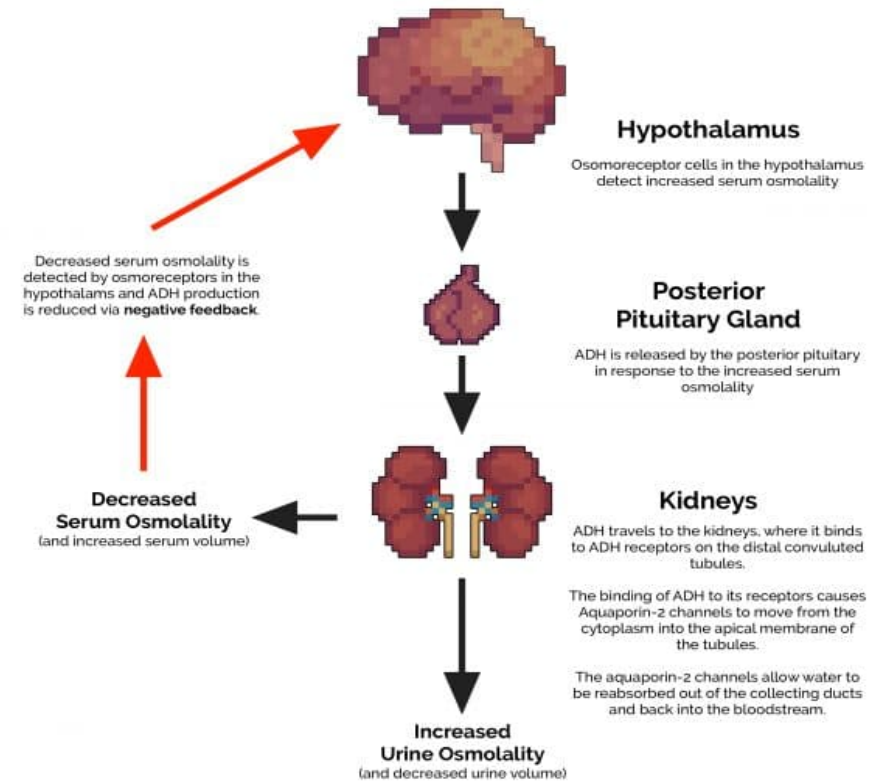

Illustration of how serum osmolality is regulated in healthy individuals.

Impaired Physiology

The fundamental difference between normal physiology and what occurs in SIADH is the lack of an effective negative feedback mechanism. This results in a continued production of ADH, independent of serum osmolality.

Ultimately, this results in an abnormally low serum sodium level and a relatively high urinary sodium level, which leads to the characteristic clinical features associated with SIADH. The fundamental difference between normal physiology and what occurs in SIADH is the lack of an effective negative feedback mechanism. This results in the continued production of ADH, independent of serum osmolality.

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Etiology:

The most common type of SIADH occurs secondary to another disease process elsewhere in the body. Hereditary SIADH, also known as nephrogenic SIADH, has been attributed to gain-of-function mutations in the vasopressin 2 (V2) receptors in the kidneys.

Conditions that often lead to SIADH

Central nervous system disorders:

Any abnormality in the central nervous system (CNS) can increase the secretion of ADH from the pituitary gland and lead to SIADH. These disorders include stroke, Guillain-Barré syndrome, multiple sclerosis, hydrocephalus, cerebral hemorrhages, infections such as meningitis, trauma, brain tumors, and even mental illnesses and psychosis.

Malignancies:

Small cell lung cancer (SCLC) is the most common tumor that leads to inappropriate production of ADH. Less commonly, extrapulmonary small cell carcinomas, head and neck cancers, and olfactory neuroblastomas also cause inappropriate release of ADH.

Drugs:

A number of drugs associated with SIADH work by increasing the release or action of ADH. The most common drugs include carbamazepine, oxcarbazepine, chlorpropamide, cyclophosphamide, and selective serotonin reuptake inhibitors (SSRIs). Carbamazepine and oxcarbazepine act in part by increasing sensitivity to ADH. Chlorpropamide increases the number of V2 receptors in the collecting ducts. Because high-dose intravenous cyclophosphamide is given with fluid loading to prevent hemorrhagic cystitis, SIADH is a particular problem in such patients, leading to potentially fatal hyponatremia. SSRIs cause SIADH by an unknown mechanism, but people over 65 years of age are at greater risk. "Ecstasy" (methylenedioxymethamphetamine), a drug of abuse, has been particularly associated with direct release of ADH. (It also causes thirst, which worsens hyponatremia.) Less commonly, nonsteroidal anti-inflammatory drugs

NSAIDs, opioids, interferons, methotrexate, vincristine, vinblastine, ciprofloxacin, haloperidol, and high-dose imatinib have been associated with SIADH.

Surgery:

Surgical procedures are often associated with excessive ADH secretion, a response likely mediated by pain afferents.

Pulmonary diseases:

Pulmonary diseases, especially pneumonia (viral, bacterial, tuberculosis), can lead to SIADH by unknown mechanisms. A similar reaction has been observed rarely in patients with asthma, atelectasis, acute respiratory failure, and pneumothorax, and sarcoidosis.

TABLE 53-1 Causes of the Syndrome of Inappropriate Antidiuresis (SIAD)

MALIGNANT DISEASES	PULMONARY DISORDERS	DISORDERS OF THE CENTRAL NERVOUS SYSTEM	DRUGS	OTHER CAUSES
Carcinoma	Infections	Infection	Drugs that stimulate release of AVP or enhance its action	Hereditary (gain-of-function mutations in the vasopressin V_2 receptor)
Lung	Bacterial pneumonia	Encephalitis	Chlorpropamide	Idiopathic
Small cell	Viral pneumonia	Meningitis	SSRIs	Transient
Mesothelioma	Pulmonary abscess	Brain abscess	Tricyclic antidepressants	Endurance exercise
Oropharynx	Tuberculosis	Rocky Mountain spotted fever	Clofibrate	General anesthesia
Gastrointestinal tract	Aspergillosis	AIDS	Carbamazepine	Nausea
Stomach	Asthma	Bleeding and masses	Vincristine	Pain
Duodenum	Cystic fibrosis	Subdural hematoma	Nicotine	Stress
Pancreas	Respiratory failure associated with positive-pressure breathing	Subarachnoid hemorrhage	Narcotics	
Genitourinary tract		Cerebrovascular accident	Antipsychotic drugs	
Ureter		Brain tumors	Ifosfamide	
Bladder		Head trauma	Cyclophosphamide	
Prostate		Hydrocephalus	Nonsteroidal anti-inflammatory drugs	
Endometrium		Cavernous sinus thrombosis	MDMA ("Ecstasy", "Molly")	
Endocrine thymoma		Other	AVP analogues	
Lymphomas		Multiple sclerosis	Desmopressin	
Sarcomas		Guillain-Barré syndrome	Oxytocin	
Ewing's sarcoma		Shy-Drager syndrome	Vasopressin	
		Delirium tremens		
		Acute intermittent porphyria		

Abbreviations: AVP, vasopressin; MDMA; 3,4-methylenedioxymethamphetamine; SSRI, selective serotonin reuptake inhibitor.

Source: From DH Ellison, T Berl: The syndrome of inappropriate antidiuresis. N Engl J Med 356:2064, 2007. Copyright © 2007 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Hormone deficiencies:

Both hypopituitarism and hypothyroidism may be associated with hyponatremia and syndrome of excessive antithyroid hormone secretion (SIADH), which can be corrected by hormone replacement.

Hormone administration:

SIADH Can be induced by administering exogenous hormones, such as vasopressin (to control gastrointestinal bleeding), desmopressin (dDAVP, to treat von Willebrand disease, hemophilia, or platelet dysfunction), and oxytocin (to induce labor). All three act by increasing the activity of vasopressin-2 (V2; antidiuretic) receptors.

Human immunodeficiency virus (HIV) infection

A common laboratory finding seen in HIV infection, whether with acquired immunodeficiency syndrome (AIDS) or with early symptomatic HIV infection, is hyponatremia. This may be due to SIADH, or it may be due to volume depletion secondary to adrenal insufficiency or gastrointestinal lesions. Pneumonia, due to Pneumocystis carinii or other organisms, and CNS infections by opportunistic pathogens are also responsible for SIADH.

Hereditary SIADH:

Mutations in the renal V2 receptor gene (located on the X chromosome) are responsible for hereditary SIADH. Such mutations lock the renal V2 receptors in a persistently active state, leading to excessive water reabsorption and hyponatremia that is resistant to vasopressin receptor antagonists.

Epidemiology:

The incidence of SIADH increases with age, but recently, the incidence of SIADH has been reported to be higher in children. Older children and adults are more likely to develop hyponatremia, especially when hospitalized for respiratory and CNS infections such as pneumonia or meningitis. SIADH is also more common in hospitalized patients and after surgery due to the administration of hypotonic fluids, medications, and the body's response to stress.

Pathophysiology:

ADH, also known as arginine vasopressin, is produced in the hypothalamus and stored in the posterior pituitary gland via the posterior pituitary stalk. The primary function of ADH is osmoregulation. However, a severe reduction in effective blood volume switches the function of ADH to volume regulation, even at the cost of a loss of effective plasma osmolality or tonicity. “Plasma osmolality” should be distinguished from “effective plasma osmolality” or “plasma tonicity,” as the latter is determined by effective osmoles in the extracellular fluid (ECF), such as sodium (which does not freely diffuse across cell membranes), the major component of ECF. Glucose and urea also increase plasma osmolality, but these are ineffective osmoles because they freely diffuse across cell membranes and do not contribute to the maintenance of plasma tonicity.

Osmotic regulation

The most important and main function of ADH is to maintain plasma tonicity, which is carried out mainly through changes in water balance. Osmotic receptors detect changes in effective plasma osmolality in the

hypothalamus. A decrease in tonicity inhibits the release of ADH and prevents water retention. An increase in tonicity causes the release of ADH, which acts on V2 receptors on the luminal surface of cortical and medullary collecting tubule cells. Under the influence of ADH, unique aquaporin-2 water channels are formed by the fusion of preformed cytoplasmic vesicles in the tubule cells, and water is absorbed in the direction of the concentration gradient. After water absorption, these channels are removed by endocytosis and returned to the cytoplasm. Osmotic receptors are very sensitive and respond to changes in plasma tonicity by as little as 1%. [6] The osmotic threshold for ADH release in humans is approximately 280–290 mOsmol/kg. Below this level, circulating ADH levels are low, and urine should be diluted to an osmolality below 100 mOsmol/kg as much as possible. Above the osmotic threshold, there is a relatively linear increase in ADH secretion. The system is so efficient that plasma osmolality does not usually change by more than 1–2%, despite large fluctuations in water intake. In patients with SIADH, ADH levels are high even in the presence of decreased plasma osmolality and/or hyponatremia. Excessive water absorption maintains high or normal blood volume.

Volume regulation

A severe drop in blood pressure sensed by "volume receptors" rather than "osmotic receptors" triggers the release of ADH (along with other hormones such as renin and epinephrine) which causes free water reabsorption from the kidneys. This can potentially lead to hyponatremia and a decrease in the effective osmolality of the ECF. Therefore, the main focus in rapid and/or significant reductions in blood volume is "volume regulation", even at the expense of decreased osmolality. This effect is more pronounced in patients with liver disease or heart disease, and hyponatremia in such patients is a direct predictor of a worse prognosis

Clinical signs:

The symptoms may be mild and vague at first. Severe cases may include these symptoms:

Irritability and restlessness, loss of appetite, muscle cramps, nausea and vomiting, muscle weakness, confusion, hallucinations, personality changes, seizures and coma

Specifically, in our case, muscle weakness was very evident after a walk accompanied by muscle cramps and restlessness, which was followed by He was in a semi-coma state, and when he was sent to the trauma hospital for the second time, the patient went into a semi-coma in a short time and then into a full coma ...

Case Report

What motivated me to report this case was its rarity. I had read about this case in textbooks and had never experienced it myself, especially since the severity of the skull injury did not indicate the extent of the occipital bone fracture and the necessary examinations with CT scan and contrast did not show serious lesions. The patient was 70 years old, athletic, with no serious or uncontrolled diseases. Especially when, after ten days, he was sent to the emergency department of the trauma hospital with a headache and especially in a semi-coma, this concern came to mind that a new hemorrhage had probably occurred. However, when they saw that there was no new brain lesion and at the same time the patient had gone into a coma, it was emphasized that it could be a disorder in the secretions and esophagitis or antidiuretic hormone, which especially after conducting blood tests for electrolytes and a severe drop in sodium levels, further proved that the patient's problem must be a disorder in the posterior pituitary. It was also a question for me when I saw that the antidiuretic hormone clearly caused serious changes in the reduction of sodium and chloride electrolytes. Even in the first days, these tests were performed twice a day, and despite the fact that the patient was being treated with normo-saline serum and even took two sodium chloride tablets three times a day, the numbers still showed the lowest numbers. The sodium range was between 120-126 m.mol was reported. At the beginning of the patient, the 24-hour urine osmolality report was as follows:

- Urine potassium 48 mmol
- Urine chloride 525 mmol
- Urine sodium 570 mmol
- 24-hour urine volume 3300 cc

Furosemide tablets and Aldactone tablets were used for this patient, but they did not continue for more than ten days.

This situation for ten days without the slightest change in their increase raised doubts that the initial diagnosis may not be correct, but after two weeks, when the patient's general condition improved, all these doubts disappeared.

History and physical condition:

Clinical manifestations of SIADH can be due to hyponatremia and decreased ECF osmolality, which causes water to move into the cells and cause cerebral edema. Signs and symptoms depend on the degree and severity of hyponatremia and the degree of cerebral edema. The first clinical manifestations of acute hyponatremia include nausea and malaise, which may occur when the serum sodium concentration falls below 125 to 130

mEq/L (normal range 135 to 145 mEq/L). Vomiting is an ominous sign in patients with acute hyponatremia. With more severe and acute decreases in sodium concentration, headache, lethargy, confusion, and eventually seizures can occur. If the serum sodium level falls below 115 to 120 mEq/L, coma and respiratory arrest can occur. Acute hyponatremic encephalopathy may be reversible, but permanent neurological damage or death, especially in premenopausal women, can occur. Chronic hyponatremia allows cerebral adaptation, and patients remain asymptomatic despite serum sodium concentrations below 120 mmol/L. Nonspecific symptoms such as nausea, vomiting, gait disturbances, memory, cognitive problems, fatigue, dizziness, confusion, and muscle cramps can occur with chronic hyponatremia. Signs and symptoms of either mild or chronic hyponatremia are often minor and are overlooked during history taking and physical examination. Nausea and vomiting occur in approximately one-third of patients with chronic hyponatremia whose serum sodium concentration is <120 mmol/L,

Diagnostic criteria:

1. Hypotonic hyponatremia
2. Urine osmolality > plasma osmolality (<275 mOsm/kg) (i.e., concentrated urine in the presence of hypotonic blood)
3. Urine sodium >20 mmol/L
4. Normal renal, hepatic, cardiac, pituitary, adrenal, and thyroid function
5. ADH testing, but accurate levels are very difficult to obtain. According to the University of Rochester Medical Center, normal ADH levels are between 0 and 5 picograms per milliliter. Higher levels can be due to SIADH. Most cases of SIADH are accurately diagnosed using measurements of blood and urine sodium and osmolality, as well as clinical observations.

Schwartz and Barter in 1967 proposed a clinical criterion that is still valid

Schwartz and Barter clinical criterion

- Serum sodium <135 mEq/L
- Serum osmolality <275 mEq/kg
- Urine sodium >40 mEq/L (due to free water reabsorption from the renal collecting ducts mediated by ADH)
- Urine osmolality >100 mEq/kg
- No clinical evidence of volume depletion - normal skin turgor, blood pressure within reference range

- No other causes of hyponatremia - adrenal insufficiency, hypothyroidism, heart failure, pituitary insufficiency, salt-excreting kidney disease, liver disease, drugs that impair renal water excretion.
- Correction of hyponatremia with fluid restriction

Relative function tests and random blood sugar tests are necessary to check for hyperglycemia and uremia, as these are potential causes of false hyponatremia.

Treatment:

The first step in treating this condition is to restrict fluid intake to prevent further fluid accumulation in the body. Medications used for this condition may include medications that reduce fluid retention, such as furosemide (Lasix), and ADH-inhibiting medications, such as demeclocycline. Any underlying medical conditions should be treated

Prognosis:

Results from conditions that are associated with The problem depends on how severe it is. Sodium deficiency that occurs rapidly, in less than 48 hours (acute hyponatremia), is more dangerous than sodium deficiency that develops slowly over time. When sodium levels drop slowly over days or weeks (chronic hyponatremia), brain cells have time to adjust, and acute symptoms such as brain swelling do not occur. Chronic hyponatremia is associated with nervous system problems such as poor balance and memory. Many causes of SIADH are reversible. Rapid correction of chronic hyponatremia can also cause dangerous complications (osmotic demyelination).

Conclusion:

In the case you saw reported, the doctors faced two challenges:

A. To package the case as a concussion case and leave it as such because the CT scan of the brain was almost normal and acceptable, and to interpret the patient's recovery over time.

B. Since the patient did not have clinical signs and symptoms related to the anterior pituitary, they ignored the lesions of the posterior pituitary, which is considered the most important and main challenge in diagnosis and, consequently, in early treatment. While it was later proven that the posterior pituitary was damaged due to trauma to the occipital bone, and for this reason, antidiuretic hormone was actually at the center of these disorders, which ultimately led to SIADH, especially since the patient had changed from a relatively good condition, within 48 hours, to delirium and even coma. The diagnoses were based on specific measurements

of 24-hour urine osmolality and blood electrolytes on two or three specific occasions. In addition, the necessary examinations for other organs possibly involved in this issue, such as the thyroid, adrenal gland, liver, and pituitary, were sufficiently examined and were reported to be completely normal.

References

- https://my.clevelandclinic.org/health/diseases/23976-siadh-syndrome-of-inappropriate-antidiuretic-hormone-secretion
- https://www.ncbi.nlm.nih.gov/books/NBK507777/
- https://medlineplus.gov/ency/article/000314.htm
- https://digidaroo.org/siadh/
- https://emedicine.medscape.com/article/246650-overview
- https://www.google.com/search?q=Yasir%253B%2BOren%2BJ.%2BMechanic.%26oq%3DSyndrome%2Bof%2BInapp
- https://my.clevelandclinic.org/health/diseases/23976-siadh-syndrome-of-inappropriate-antidiuretic-hormone-secretion
- https://litfl.com/siadh-syndrome-of-inappropriate-adh-secretion/
- Harrisons-Principles-of-Internal-Medicine-2022-21st-edition

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