CLINICAL VIGNETTE

A Spontaneous Case of Central Diabetes Insipidus

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Case Presentation

A 57-year-old woman presented with 2-months of dry mouth and polyuria. Symptoms developed acutely and also included dry eyes and fatigue. She had increased her water intake to 40 cups per day and noted decreased appetite for solid foods due to dysphagia. She was previously healthy with no history of autoimmune disease, arthralgias or rash. She did complain of increased stress around the time of symptom onset.

On physical exam, vital signs including blood pressure were normal. Her general appearance and rest of her physical exam was completely normal.

She had normal saliva production and normal lab testing to rule autoimmune diseases.

Laboratory evaluation included normal TSH 1.5 mIU/L, A1c 5.5 mg/dL, prolactin 12.8, ACTH 25, growth hormone 0.1, and cortisol. Arginine vasopressin was low < 1.0 (normal 1.0 – 13.3), sodium mildly elevated at 146, and normal urine Specific Gravity (SG) of 1.005.

MRI of the pituitary found less hyperintensity in the posterior pituitary, without obvious posterior pituitary mass or infiltrative process. The pituitary stalk was normal in size and enhanced normally.

The patient was referred to endocrinology and had overnight water deprivation test. The results were consistent with central DI, with sodium of 154 mEq/L and urine SG < 1.005. The cause of central diabetes insipidus was unclear.

She was started on DDAVP 0.1 mg bid with plan to repeat the pituitary imaging.

Follow up labs included normal TSH, cortisol, ACTH E2 < 12, FSH 40 LH 18, prolactin 13 Na 140 mEq/L, ACE 18.

Repeat MRI 4 months later showed the hypoenhancing focus in the right posterior pituitary gland was stable and felt to represent incidental pituitary microadenoma.

She has been maintained in DDAVP 0.5mg T.I.D. Her labs have remained normal including prolactin, sodium, and urine S.G. MRI of the pituitary has also been stable over several years.

Discussion

Normally, the hypothalamus secretes antidiuretic hormone (ADH) which acts on the kidneys to control the amount of fluid that is secreted by the kidney in order to regulate fluid homeostasis and electrolyte levels. Central Diabetes Insipidus (central DI) is caused by an insufficiency of antidiuretic hormone (ADH), and can be due to deficits in the hypothalamic osmoreceptors, supraoptic/paraventricular nuclei, or supra-opticohypophyseal tract. As in this case, approximately 30-50% of cases are idiopathic, due to damage to the hypothalamic nuclei, while others are due to tumors or infiltrative diseases including metastasies, Myelodysplastic Syndrome, or Langer-hans cell Histiocytosis, autoimmune causes such as IgG4 related syndromes, granulomatosis with polyangiitis; surgery, hypoxic encephalopathy, or trauma.[1] Transient decrease in ADH release can also be seen in patients after supraventricular tachycardia and in patients with anorexia nervosa.

Clinical Manifestations

Most commonly patients will have polyuria, nocturia, and polydipsia. As in our patient, the serum sodium is often high-normal. Some patients may also have decreased bone density. Adult onset of central DI is usually abrupt, whereas nephro-genic DI or primary polydipsia is usually more gradual.

Diagnosis

In patients with suspected polyuria and normal serum sodium, there are a variety of techniques proposed. The combination is detailed and summarized below.[2-4]

1) Rule out obvious causes of solute/osmotic diuresis such as glucose, sodium, urea, mannitol, etc. Then, collect a 24-hour urine to confirm polyuria defined as >3L/day along with urine osmolality, creatinine, sodium, potassium, chloride, urea nitrogen, and glucose. Concurrently check plasma electrolytes, glucose, creatinine, and blood urea nitrogen. If the urine osmolality is >600 mosmol/kg, or if daily osmolar output (urine Osmolality x 24 hr urine volume) is > 1000 mosmol, then the patient has solute/osmotic diuresis.[4]
2) Otherwise, the next step is to rule out nephrogenic diabetes insipidus. If the patient has an obvious cause such as bilateral urinary tract obstruction, persistent hypercalcemia, or family history of nephrogenic DI,

then the diagnosis should be confirmed with a desmopressin challenge and observed for an expected rise in urine osmolality or plasma copeptin.[5]

3) The next step is to rule out primary polydipsia with an overnight water restriction test. Rise in urine osmolality to >700 mosmol/kg with avoidance of water overnight, establishes the diagnosis of primary polydipsia. However, serum sodium concentration of >145meq/L and serum osmolality of >295 mosmol/kg with water restriction (or hypertonic saline) is needed to distinguish central DI from polydipsia. Patients with severe polyuria and urine osmolality <100 mosmol/kg who likely have complete DI should not undergo overnight water restriction for safety reasons.
4) Once plasma sodium concentration of > 145 has been achieved, desmopressin is given along with measurement of plasma copeptin levels. Copeptin is a precursor molecule to ADH in the body and can be used as a surrogate marker for endogenous productions of ADH. The change of urine osmolality as well as the copeptin levels will determine the diagnosis.

    a. Complete DI, if urine osmolality more than doubles.
    b. Partial central DI, if urine osmolality rises 15-100% to a value >300 mosmol/kg. This can be supported by low copeptin levels
    c. Partial or complete Nephrogenic DI, if urine osmolality rises up to 45% to a value <300 mosmol/kg.

Treatment

Although the general principle of treatment is to supplement the Antidiuretic Hormone (ADH, also called Arginine Vasopressin or AVP/DDAVP), care must also be taken to replace prior and ongoing fluid losses. Most patients with intact cognition, thirst drive, and physical ability will increase fluid intake to supplement losses, but hypernatremia and dehydration can occur in those without ready access to water. In central DI, the urine osmolality is generally fixed due to lack of ADH. Urine volume is therefore directly related to solute intake as the thirst drive will normally result in sufficient fluid intake to keep the serum osmolality within range. That is why in milder cases of central DI, solute restriction and a thiazide diuretic to promote excretion of sodium may be sufficient to control symptoms.

Other patients with more severe cases or patients unable to undergo a solute restriction diet/diuretics, treatment with Desmopressin an analogue of ADH is preferred. Since the most bothersome symptom of DI is generally nocturia, treatment generally starts with night time administration of desmopressin. Since an intact thirst reflex is present to counteract hypernatremia during the day, the goal of partial control of the DI during the helps balance the risk of water retention and hyponatremia. Also, since much of daily fluid intake may not be driven by thirst, with consumption of caffeinated beverages and soup, treatment with too much desmopressin can cause a situation similar to Syndrome of Inappropriate ADH (SIADH). It is recommended to monitor sodium several times in the first few days of supplementation to ensure stable levels. Treatment continues as long as DI persists.

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