Diabetes Insipidus

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Polyuria

- Polyuria: excretion of large volumes of dilute urine.
- Three main causes in the absence of hyperglycemia:
  - Primary Polydipsia
  - Central Diabetes Insipidus
  - Nephrogenic Diabetes Insipidus

Primary Polydipsia

- Often seen in the setting of psychiatric illness.
- Water intoxication – insatiable urge to drink water.
- A low plasma sodium with a low urine osmolality is a clue to water overload due to primary polydipsia.

Central Diabetes Insipidus

- Due to deficient secretion of antidiuretic hormone (ADH, also called arginine vasopressin or AVP) by the posterior pituitary.
- Most commonly autoimmune or idiopathic.
- Can be due to trauma, pituitary surgery, hypoxic or ischemic encephalopathy.
- Onset of central DI in adults is usually abrupt.
- A high normal plasma sodium with low urine osmolality is a clue to DI.

Antidiuretic Hormone (ADH)

- ADH (also called arginine vasopressin or AVP) is a polypeptide hormone produced in the hypothalamus and stored in the posterior pituitary.
- ADH is released from the posterior pituitary into the systemic circulation under the control of osmoreceptors in the hypothalamus, and volume receptors in the neck vessels and heart. Volume stimuli always override osmotic stimuli.
- ADH acts on the kidneys to increase water reabsorption; ADH can also increase vascular resistance.

Hypernatremia

- In a patient with DI who is cognitively intact with an intact thirst mechanism and ready access to water, hypernatremia will not occur because the patient will become thirsty and will drink sufficient water to keep up with the water loss. Patients might complain of getting up every hour all night.
- A patient with DI who is not cognitively intact, or who lacks a thirst mechanism (adipsic DI), or who cannot access drinking water, can develop severe hypernatremia (> 160).

Hypernatremia

- Withholding water in a patient with DI can lead to severe hypernatremia.
- This would apply to patients with DI who are NPO for surgery or severely cognitively impaired and unable to drink. Such patients must be
  - hospitalized;
  - given adequate IV fluids with free water (such as D5W);
  - monitored with frequent measurement of sodium levels; and
  - treated with desmopressin to control urine volume.

Water Deprivation Test

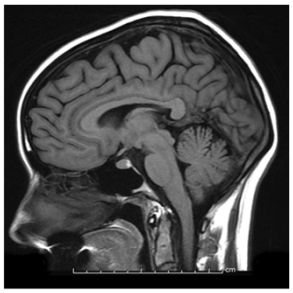
- Can be used to differentiate between primary polydipsia and central DI.
- Not necessary if sodium is already over 145 and the urine osmolality is less that half of plasma osmolality, or if the cause is clinically obvious (new onset after head trauma or pituitary surgery).
- This test must be done under very controlled conditions with stat Na levels every 2 hours.
- ADH assays are generally unreliable and require special specimen handling.

Diagnostic Considerations: Central Diabetes Insipidus

- Patients with central DI will complain of polyuria, nocturia, and polydipsia.
- An MRI of the brain and pituitary will often show lack of the posterior pituitary bright spot on T1 images. The bright spot is thought to represent stored arginine vasopressin.
- The bright spot is not always found in normal patients.
- Therefore, absence of the bright spot - in the appropriate clinical context - is suggestive of central diabetes insipidus.

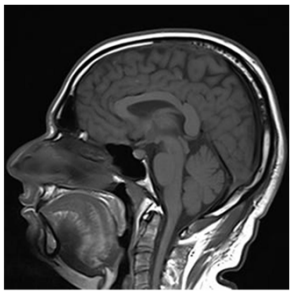
Posterior Pituitary Bright Spot

Case courtesy of A.Prof Frank Gaillard, Radiopaedia.org, rID: 9878



Case of Central DI – Absent Bright Spot

Case courtesy of Dr Gaurav Som Prakash Gupta, Radiopaedia.org, rID: 24225



Triphasic Response after Neurosurgery or Trauma

- Initial polyuric phase: beginning within 24 hours and lasting 4 to 5 days; inhibition of ADH release due to hypothalamic dysfunction.
- Days 6 to 11: antidiuretic phase - stored hormone is slowly released from the degenerating posterior pituitary; excessive water intake can lead to hyponatremia because of a transient syndrome of inappropriate ADH secretion.
- Permanent DI: may ensue after the posterior pituitary ADH stores are depleted.

Desmopressin Acetate (DDAVP)

- Desmopressin is the most frequently used agent to treat central DI.
- It is a synthetic analogue of 8-arginine vasopressin (AVP, ADH), with modifications at two amino acid positions; the first amino acid has been deaminated, and arginine at position 8 is in the *dextro* rather than *levo* form:
  - 1-(3-mercaptopropionic acid)-8-D-arginine vasopressin monoacetate (salt) trihydrate.
- Desmopressin has enhanced antidiuretic activity and decreased vasopressor activity and decreased action on visceral smooth muscle.
- Contraindicated in moderate to severe renal insufficiency.

Desmopressin Drug Interactions

- The concomitant administration of drugs that may increase the risk of water intoxication with hyponatremia, (e.g. tricyclic antidepressants, selective serotonin re-uptake inhibitors, chlorpromazine, opiate analgesics, NSAIDs, lamotrigine and carbamazepine) should be performed with caution.

Initial Treatment of Central DI

- The main goal of treatment is to reduce nocturia so the patient can sleep. Therefore treatment with desmopressin is initiated at bedtime:
- Desmopressin can be given orally as ½ of a 0.1 mg oral tablet (0.05 mg) HS; or
- Intranasally at 10 mcg HS using the metered desmopressin nasal spray; or
- Intranassally at 5 mcg (0.05 mL) HS using the desmopressin solution and a plastic rhinal tube which allows the patient to blow the solution into the nose.

Desmopressin Dose Titration

- Intranasal: gradually increase the HS dose until nocturia is controlled, and add a daytime dose if needed. The maintenance dose is usually 5 to 20 mcg once or twice a day (10 to 20 mcg once or twice a day with the metered spray).
- Oral: gradually increase the HS dose until nocturia is controlled, and add a daytime dose if needed. The maintenance dose is usually 0.1 to 0.8 mg daily in two or three divided doses.
- The dose should be titrated to relieve nocturia and to provide ***partial*** control of daytime polyuria.
- It is critical to avoid excessive dosing because that can lead to excess water retention and hyponatremia.

Hyponatremia

- Patients must be carefully counseled to avoid excessive water intake while on desmopressin. If they continue to drink the volume of water that they have become accustomed to, they will develop severe hyponatremia. They should be coached to drink free water only when thirsty.
- Patients should be educated on the symptoms of hyponatremia: nausea, vomiting, headache, lethargy, and, if severe, seizures and coma.
- Only use the minimum effective dose of desmopressin to minimize the risk of hyponatremia.

Laboratory Monitoring

- Na level should be checked one or two days after the initiation of desmopressin therapy, and if normal, again at 4 days.
- Once a stable regimen is achieved, the sodium level can be checked once or twice a year.
- All patients with central DI should have a medical alert bracelet, so the ER clinician will be aware that the patient needs desmopressin, careful fluid management, and monitoring of sodium.

Case

- 40 yo F presents with lethargy, inability to concentrate and poor memory, doing poorly at work. She gets up 4 to 5 times every night to pass urine. Drinks multiple bottles of Gatorade every day.
- GYN hx: G3P3, children healthy ages 18,14,12. After third pregnancy she could not nurse, and her periods did not return.
- What key information would you ask?
- What workup should be undertaken?