Diabetes Insipidus in a Quadriplegic Patient

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An incomplete quadriplegic patient underwent investigation for production of copious amounts of dilute urine. Serum osmolality, electrolytes, BUN, glucose, and serum antidiuretic hormone (ADH) were recorded, as well as urinary osmolality, electrolytes, glucose, and pH. In response to subcutaneous vasopressin during the dehydration test, the patient's urinary osmolality increased by 12%, from 620 mOsm/L to 695 mOsm/L. A definitive diagnosis of partial central diabetes insipidus was made. Physicians involved in the care of patients with spinal cord injuries should be aware of the method of evaluating polyuric conditions, particularly while the patient is undergoing catheterization.

KEY WORDS: Diabetes insipidus; Polyuria; Quadriplegia; Spinal cord injuries

CASE REPORT

A 32-year-old man fell from a 4-foot height, sustaining a C6-7 fracture dislocation and C7 incomplete quadriplegia. There was no associated head trauma or loss of consciousness. His medical history was positive for a benign prostatic nodule. He underwent a posterior spinal fusion with iliac crest bone graft and halo immobilization. His medical course was initially complicated by a deep vein thrombophlebitis (DVT) and pyelonephritis.

An ICP was then begun, first every four hours, then every three hours, on an 1,800 mL/d fluid restriction. He was not on salt restriction or diuretics. His residual volumes reached 600-900 mL on ICP every four hours and 500-600 mL on ICP every three hours. His total daily output ranged from 2,200-6,000 mL averaging 5,500 mL. There was no spontaneous voiding of urine. Urodynamics revealed good to normal sensation to bladder filling, with strong urge to void at 500-600 mL, but no detrusor activity. There was a hyperactive bulbocavernous reflex. A sphincter electromyogram was not performed because the patient was receiving sodium warfarin (Coumadin). Spot urine specific gravities at 10 AM and 3 PM were 1.011 and 1.002, respectively. Urines remained negative for glucose. When not infected, the patient's urinary pH ranged from 6.0-7.0. Serum electrolytes remained within normal limits, although his serum sodium was noted to climb from 135 to 143 in a 2-week period. The serum SMA-12 was unremarkable. Spot urinary electrolytes were as follows: sodium, 136; potassium, 32.7; and chloride, 32. Simultaneous random plasma and urinary osmolalities, while on 1,800 mL/d fluid restriction, were as follows:

<table>
<thead>
<tr>
<th>Plasma (mOsm/kg)</th>
<th>Urine (mOsm/L)</th>
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<tbody>
<tr>
<td>11/30/83 12 noon</td>
<td>295</td>
</tr>
<tr>
<td>12/9/83 12 noon</td>
<td>290</td>
</tr>
<tr>
<td>12/12/83 3 PM</td>
<td>292</td>
</tr>
<tr>
<td>12/13/83 9 AM</td>
<td>293</td>
</tr>
</tbody>
</table>

A spot serum ADH level, while fluid was restricted, was 1.3 pg/mL (normal < 12 pg/mL in the hydrated patient). Upon further questioning, the patient admitted to a lifelong history of nocturia (3-4 times/night) of large volumes, and of excessive thirst. His father and paternal uncle had similar histories.

The patient underwent the dehydration test as outlined by Miller and associates. He concentrated his urine to 620 mOsm/L following 18 hours without food or drink. One hour after a subcutaneous injection of vasopressin, the urinary osmolality rose to 695 mOsm/L, which was a 12% increase in urine concentration. He was begun on chlorpropamide 250 mg/d orally. Coincidentally, within two days, he began to spontaneously void. His subsequent urine outputs never rose above 3,700 mL/d, averaging 3,000 mL/d. Serum glucose remained stable.

DISCUSSION

The differential diagnosis of polyuric conditions can be approached using the method of Singer's "diagnostic decision tree." This method begins with determining whether the problem is primarily a water diuresis or a solute diuresis. A complete history of the premonitory and present drinking and voiding patterns is essential, followed by urine and serum analyses. In general, a pure water diuresis is associated with urines of low specific gravity (less than 1.005) and low osmolality (less than 200 mOsm/L). With a solute diuresis, the urinary specific gravity is usually near 1.010, and urinary osmolality is close to 300 mOsm/L.

If a solute diuresis is suspected, it must be determined which

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solute is at fault, electrolyte or nonelectrolyte. A simple urinalysis for glucose and pH can be valuable. A negative or minimally positive urinary test for glucose almost always rules out glucose as the solute responsible for ongoing diuresis. A low serum BUN will almost always rule out other nonelectrolyte solutes. A sodium salt is almost always involved in an electrolyte-induced diuresis. If the urine pH is less than 7.0, urinary sodium bicarbonate is virtually ruled out as a possible cause for ongoing solute diuresis, leaving sodium chloride as the responsible solute. No other salts or electrolytes (sodium phosphate, sodium sulfate, potassium, calcium, ammonium) normally appear, without renal failure, in sufficient quantities to produce a sustained solute diuresis. Sodium chloride diuresis is caused by excessive sodium intake (psychogenic or iatrogenic) or by excessive sodium chloride loss by the kidney as in "salt-losing" nephritis or chronic renal failure. Other causes include extra-renal hormonal deficiencies (Addison's disease) and diuretic use.

If a water diuresis is suspected, the next step is to determine if the primary problem is one of excessive input to the kidney or of excessive output from the kidney, i.e., distinguishing between primary excessive water intake and primary excessive water loss. The former is commonly associated with hypotension and clinical evidence of volume expansion. The latter is commonly associated with hypotension and clinical evidence of volume contraction. Our patient fit the pattern of volume contraction: slowly climbing serum sodiums, thirst, fatigue, weakness, and dry mucous membranes. Significant diuresis can also result from the increased effective renal blood flow in the recumbent position, as seen in our patient's higher nighttime urine volumes.

After clinical evaluation, it is helpful to perform the two-part dehydration test (urinary concentrating test) to separate the two possible types of water diuresis. The first part of the test, performed before administration of exogenous ADH to a dehydrated patient, can help distinguish excessive water input from excessive water loss. A patient with primary excessive water input should be able to concentrate the urine normally when dehydrated, whereas a patient with excessive renal water loss will not concentrate the urine normally when dehydrated.

The second part of the dehydration test begins with the administration of exogenous ADH (aqueous vasopressin). This helps to distinguish renal defects (nephrogenic DI) from extra-renal defects (central DI). Both conditions present with polyuria due to a primary water loss with a secondary polydipsia. In healthy persons, urinary osmolality never rises by more than 9% after a subcutaneous injection of vasopressin, no matter what the maximal urine osmolality might have been after dehydration alone. Any value above a 9% increase in urine concentrating ability, after vasopressin injection, represents a positive result from some degree of central DI. In pure central DI, the urinary osmolalities would be expected to stabilize at 150–200 mosM/L with dehydration, and then to increase by approximately 50% or more in response to vasopressin injection. A patient with nephrogenic DI would likewise stabilize his urinary osmolalities near 200 mosM/L after dehydration, but would not respond to vasopressin. A healthy subject would be able to concentrate his urine to a much higher osmolality with dehydration, usually at least 800 mosM/L, with minimal increase (less than 9%) in urine concentrating ability following vasopressin injection.

Our patient did not normally concentrate his urine in response to dehydration in part one of the dehydration test. This was partially corrected by 12% with exogenous ADH in part two of the test, hence the diagnosis of partial central DI.

Diabetes insipidus is a disease in which there is a deficiency of vasopressin or vasopressin effect, resulting in impaired renal conservation of water. Clinically, a patient with this disorder will present with polyuria, excessive thirst, and polydipsia. Urine outputs may reach 16–24 L/d, but usually are only moderately elevated from 2.5–6 L/d.

There are two general types of DI: nephrogenic DI (which represents a failure of the kidneys to appropriately respond to adequate levels of ADH in the bloodstream) and central DI (which represents a failure of the pituitary to synthesize or release ADH into the bloodstream).

Nephrogenic DI can be caused by an abnormality in the osmotic gradient of the renal tubules or by an abnormality in the response of the renal collecting ducts to ADH. The former has been associated with hypercalcemia, lithium, medullary or tubulointerstitial renal disease, interstitial nephritis, and nephrotoxins. The latter has been associated with hypercalcemia, lithium, congenital nephrogenic DI, and colchicine, vincristine, and methoxyflurane toxicity. The treatment of nephrogenic DI is salt restriction and thiazide diuretics. This regimen is presumed to work by decreasing the solute and water delivery to the distal nephron. This disease does not respond to hormonal treatment.

Central DI is far less common than nephrogenic DI, but it is often easier to treat. The ADH level in the bloodstream may be undetectable as in "complete" central DI, or inadequate in amount, as in "partial" central DI. Complete central DI requires hormone replacement therapy. Partial central DI may often be treated by agents that increase the release or the renal action of endogenous ADH.

There are many etiologies of central DI, including congenital idiopathic forms and idiopathic cases reported to be associated with anorexia nervosa. Most cases, however, are acquired because of disease and/or therapy in the hypothalamic-hypophyseal region. Drugs (such as Clonidine), tumors (craniopharyngiome, pinealoma, metastatic loci), or the treatment of tumors (surgery, radiation), vascular diseases, granulomatous diseases (sarcoma, tuberculosis), hemorrhages, abscesses, meningitis, and syphilis can affect this region of the brain and produce a central DI. There have also been reported cases of central DI following severe head injury, usually associated with skull fractures and typically with loss of consciousness and cranial nerve injuries.

The therapy of central DI needs to be carefully individualized. According to Singer, at one extreme are asymptomatic persons who require no chronic therapy. They may have partial DI and an intact thirst mechanism. Their mild symptoms and nocturia may not interfere with daily activities or sleep requirements. Our patient, prior to his quadriplegia, was in this situation. He did have partial central DI prior to his cervical injury. Before his injury, he had been able to void spontaneously. These patients are at risk only when they do not have free voluntary access to water, e.g., patients placed on fluid...
restriction for ICP, or are unable to communicate the need for water due to aphasia or comatose state, or have no spontaneous urination, as in the case of our quadriplegic patient. At the other extreme are severely symptomatic patients with no endogenous ADH activity and a defective thirst mechanism. The treatment of choice for complete central DI is DDAVP (1-desamino-8-d-arginine vasopressin), a synthetic analog of natural human ADH (arginine vasopressin). It is long-lasting with low pressor activity. It is marketed in a convenient nasal spray form for once-a-day use; however, the cost may be prohibitive for chronic use.

Partial central DI need not be treated with hormone therapy, but can respond to less expensive nonhormone therapy. Chlorpropamide (Diabinese) 250–750 mg/d orally is effective by enhancing the renal action of small amounts of circulating endogenous ADH, and probably also enhances the release of additional ADH from the pituitary. Clofibrate (Atromid-S) 500 mg every six to eight hours, orally will also work by increasing the release of endogenous ADH into the bloodstream. Our patient was begun on chlorpropamide because of cost, easy availability, and once-a-day dosage. Surprisingly, secondary hypoglycemia is rare in central DI patients treated with chlorpropamide (Adlin V: personal communication).

### SUMMARY

This paper presents a unique case of a patient who, by history, had diabetes insipidus preceding a spinal cord injury (SCI). He had remained essentially unscathed by the DI until his injury rendered him unable to spontaneously empty his bladder. The disease state caused his ICP to be totally unmanageable. The literature of the past 20 years reveals no other reported cases of premorbid DI detected in a patient with spinal cord injury.

The differential diagnosis of polyuric states depends on obtaining a thorough history, as well as the answers to a few basic physiologic questions. The important first step is distinguishing a water diuresis from a solute diuresis. From that point, a few noninvasive laboratory tests can aid the physician in narrowing the diagnostic possibilities. In a patient with a spinal cord injury and a neurogenic bladder, the recognition and treatment of the problem are even more crucial, so that adequate bladder tone is preserved and urinary reflux avoided.

### ABSTRACTS of selected literature


- The effect of muscle length on susceptibility to fatigue has been examined in human ankle dorsiflexor muscles. The fatiguing procedure consisted of either indirect tetanic stimulation at 20 Hz or maximal voluntary contraction; each procedure lasted 90 s. The amplitude of the evoked muscle compound action potential (M-wave) increased during the first 30 s or so of the tetanic fatiguing procedure and then decreased. The torque developed by the dorsiflexor muscles declined throughout the period of tetanization. A significantly greater reduction in twitch and tetanic torque was found after the fatiguing procedure had been conducted at the optimum muscle length rather than with the muscle in a shortened position. Relaxation after tetanic stimulation was slower after fatigue had been induced at the optimum muscle length. It is concluded that muscle fatigue is related to the number of actin-myosin cross-bridge interactions and is unlikely to be accounted for solely on the basis of changes in the ionic composition of the transverse tubular fluid.


- The aim of the study was to determine the fibre size distribution within the human m. tibialis anterior. Ten-micron thick cross-sections of the whole muscle were enzyme histochemically stained for myofibrillar ATPase at pH 9.4. The cross-sectional area of 100 fibres with low (type 1) ATPase and high (type 2) ATPase activity was measured in three different regions (superficial, central and deep). Both the type 1 and type 2 fibres were found to be larger in the deep region than in the central or superficial regions. The variation in fibre size could not be explained by the cryofixation or cryo-embedding techniques used. The data suggest that muscle adaptation to physical demands may not only occur by means of variation in types and number of muscle fibres, but also by variation in fibre size over the muscle cross-section.

References