The Man Who Drank Too Much

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A 35-year-old male presents with excessive thirst and urination of abrupt onset which he dates back to getting married 2 years ago. He awakens to drink and urinate 5 times nightly. There is no other significant medical or family history. Results on physical exam were unremarkable. Serum electrolytes, urea, creatinine, calcium, phosphate, and liver function tests were all within normal limits. Urine analysis revealed low specific gravity and osmolality, at 1.005 (Normal: > 1.015) and 190 mOsm/kg (Normal: 700 – 1400 mOsm/kg) respectively (1).

Q1: What would be your differential diagnosis for this patient?
Q2: How would you distinguish amongst the polyuric syndromes?

A1: A brief list of causes for polyuria is shown below.

Major polyuric syndromes (2)

I. **Primary disorders of water intake or output**

A. **Excessive water intake**

Psychogenic polydipsia

Drug-induced polydipsia (Thioridazine, Chlorpromazine, Anticholinergics)

B. **Inadequate tubular reabsorption of filtered water**

Vasopressin (ADH) deficiency

a Neurogenic DI

b Drug-induced inhibition of ADH release ex) Narcotic antagonists

Renal tubular unresponsiveness to ADH

a Nephrogenic DI (congenital and familial)

b Nephrogenic DI (acquired)

(1) Chronic renal disease, obstructive uropathy, unilateral renal arterial stenosis, post renal transplantation, chronic pyelonephritis

(2) Hypokalemia

(3) Chronic hypercalcemia

(4) Drug-induced: lithium, methoxyflurane anesthesia, demeclocycline

(5) Various systemic disorders: multiple myeloma, amyloidosis

II. **Primary disorders of renal absorption of solutes (osmotic diuresis)**

A. **Glucose: diabetes mellitus**

B. **Salts, especially sodium chloride**

Various chronic renal diseases, especially chronic pyelonephritis

After various diuretics, including mannitol

A2: The causes for polyuria can often be elicited by a thorough history including recent medications and procedures. Routine blood work and a urine sample are helpful to exclude diabetes mellitus and other electrolye abnormalities.

If the etiology remains uncertain, a number of specialized tests can be used to differentiate between excessive water intake, neurogenic DI, and nephrogenic DI. In these tests, the plasma osmolality is purposely elevated by either fluid deprivation or hypertonic saline infusion. The key to correct interpretation of these tests lies in the association between urine and serum osmolality. Urine osmolality values that remain inappropriately low as the serum osmolality rises suggest DI. A vasopressin challenge, whereby a subject is given intravenous vasopressin, can differentiate neurogenic DI from nephrogenic DI. Urine osmolality incresases markedly in the former, but does not rise in the latter. These tests must be done under carefully monitored conditions to ensure those patients with psychogenic polydipsia do no ingest water, and those with DI do not become critically volume depleted.

If a clinical and biochemical diagnosis of neurogenic DI is made and the etiology cannot be determined from the history and physical examination, radiologic investigations (by either CT or MRI) can be performed to rule out a hypothalamic tumor (1).

Q3: An MRI was done on this patient and a midline sagittal T1-weighted image is shown below (Fig. 1). What is the abnormality? For comparison a normal sagittal T1-weighted image is shown in Fig. 2.

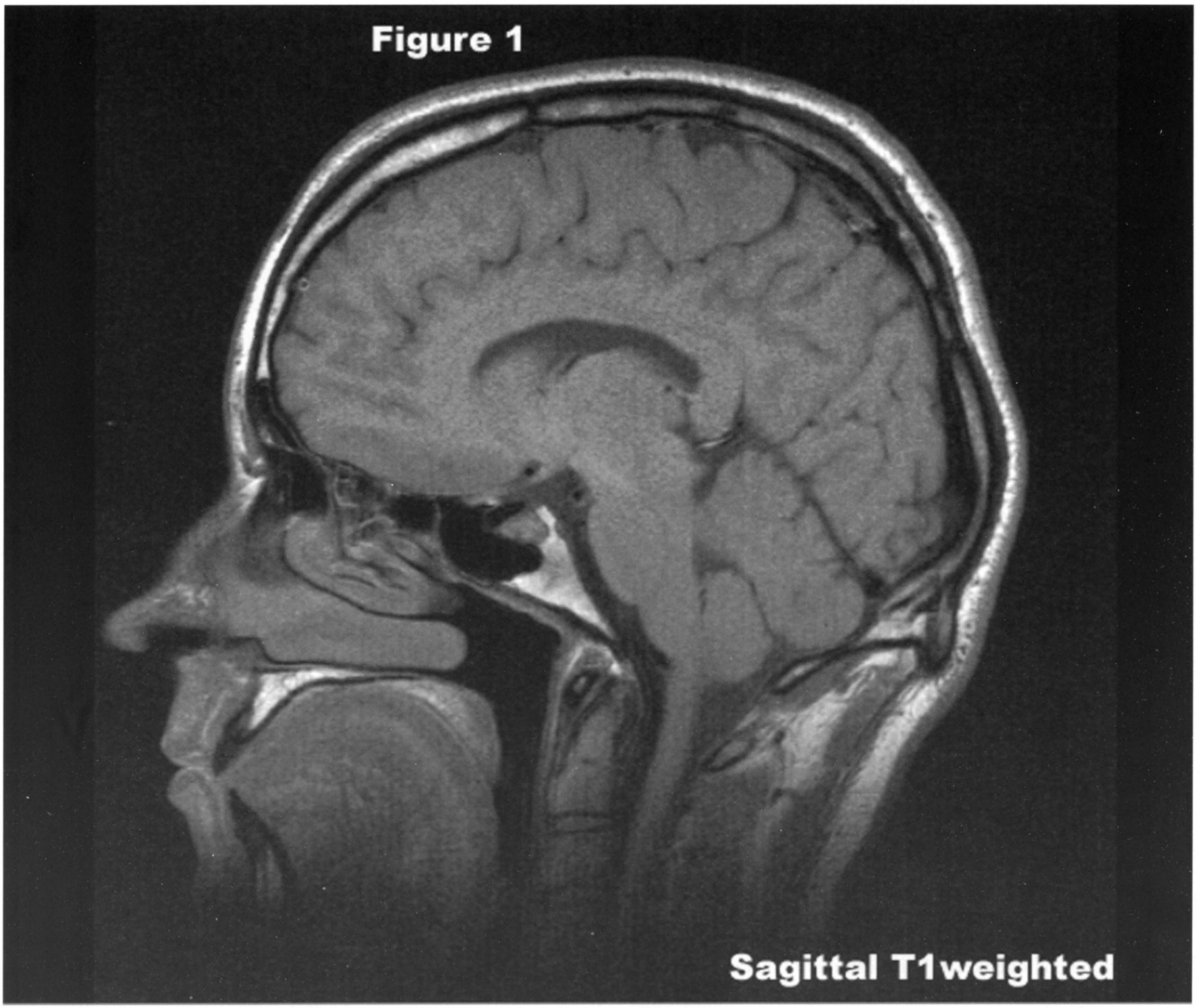

Figure 1: Midline Sagittal T1-weighted MRI

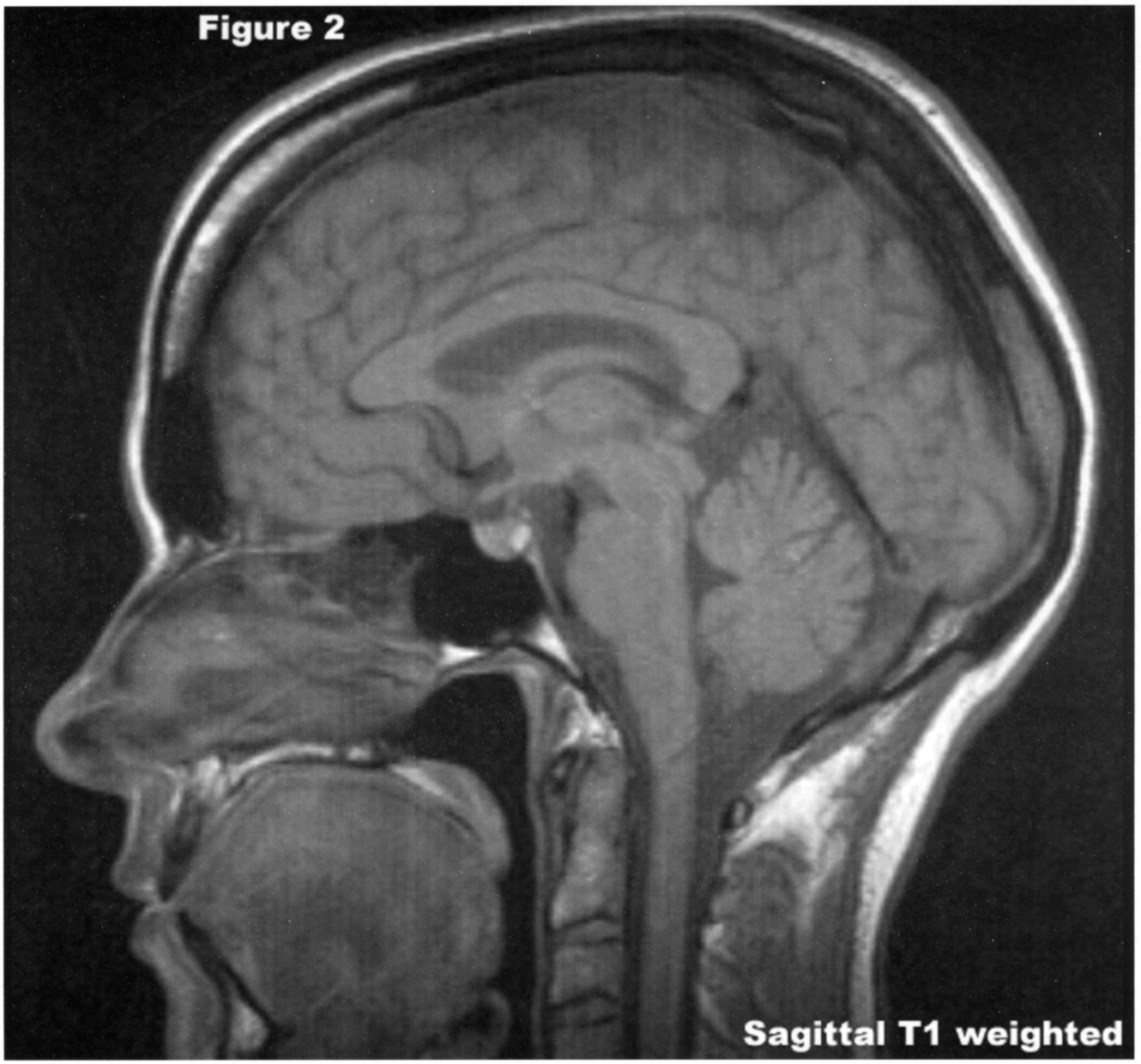

Figure 2: MRI of Normal Individual

A3: Found in the posterior pituitary stalk, the storage site for vasopressin appears as a hyperintense area on T1-weighted images (3). The size of the hyperintense area, or "bright spot", appears to be related to the functional state of the neurohypophysis, being absent in patients with clinical symptoms of neurogenic DI (3). However, since the "bright spot" may not be seen in 10 to 20 percent of normal patients, failure to visualize it on routine cranial MR images should not be viewed as evidence of neurohypophysial disease (4). Failure to visualize is thought to be due to the thickness of the cuts and volume of averaging of signal from surrounding fluid (3).

The absence of signal in the patient's posterior pituitary is the only abnormality. No neoplastic, vascular, or post-surgical changes are seen. By exclusion, idiopathic DI is the diagnosis.

Diagnosis: Idiopathic Neurogenic Diabetes Insipidus

Neurogenic DI frequently starts in childhood or early adult life and is more common in males than females (2). The major causes are as follows:

Idiopathic DI accounts for approximately one-quarter of cases of DI (5). This usually starts in childhood and is seldom associated with anterior pituitary dysfunction. This diagnosis is made by exclusion of all other causes.

Neoplastic lesions of the hypothalamus or pituitary, including craniopharyngiomas, germinomas, and metastatic tumors.

Pituitary or hypothalamic surgery which usually develops within one week following surgery and may become chronic.

Severe head injury is usually associated with fractures of the skull.

Vascular lesions may rarely cause DI. Causes include: shock, Sheehan's syndrome, and aneurysms.

Familial/Congenital DI is a rare hereditary form that is transmitted as an autosomal dominant trait (1).

In neurogenic DI, the posterior pituitary fails to secrete adequate amounts of vasopression, or antidiuretic hormone (ADH), in response to osmotic stimuli. This reduction in ADH results in a decrease in urine osmolality and a reciprocal rise in the rate of urine flow. However, only 10-20% of the neurohypophysis is required to maintain normal function (6). Symptoms of excessive thirst and polyuria are compensatory measures when there is less than this.

Severe DI occurs when ADH secretory capacity declines to the point where an abnormally intense stimulus fails to elicit adequate ADH secretion for urinary concentration (6). If severe dehydration ensues, patients may exhibit weakness, fever, psychic disturbances, hypotension, tachycardia, prostration, and death (2). Any patient with DI who is excessively fluid restricted may develop hypertonic encephalopathy when the serum osmolality exceeds 350 mOsm per kg (1). In an acute hyperosmolar state, the central nervous system experiences rapid shifts of water giving mental status changes and neurologic symptoms, in addition to marked dehydration (1).

Intranasal or oral desmopressin acetate (DDAVP), a synthetic analog of ADH, is typically the drug of choice in the treatment of patients with neurogenic DI (1,2). The severity of the disease determines the frequency of administration of DDAVP. Adequacy of replacement is monitored by regular measurement of serum osmolality and sodium. Patients with some residual releasable ADH may respond to treatment with several nonhormonal agents, including: chlorpropamide, clofibrate, and carbamazepine (1,2). These agents work by stimulating release of ADH. Patients with milder forms of neurogenic DI may merely require adequate hydration.

REFERENCES

1. Moses AM, Streeten DHP. Disorders of the Neurohypophysis. In: Fauci AS, Braunwald E, Isselbacher RS, et al., eds. Harrison's Principles of Internal Medicine. 13th ed. New York: McGraw-Hill, 1998: 2003-2012.
2. Adam P. Evaluation and management of diabetes insipidus. Am Fam Physician 1997; 55(6): 2146-53.
3. Elster AD. Imaging of the sella: anatomy and pathology. Semin Ultrasound CT MR 1993; 14: 182-94.
4. Brooks BS, El Gammal T, Allison JD, et al: Frequency and variation of the posterior pituitary bright signal on MR images. AJNR 1989; 10: 323-328.
5. Moses AM. Clinical and laboratory observations in the adult with diabetes in sipidus and related syndromes. Front Horm Res 1985; 13: 156-75.
6. Robertson GL. Diabetes insipidus. Endocrinol Metab Clin North Am 1995; 24: 549-72.