

An unquenchable thirst

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Mr. F, age 44, has schizophrenia that includes religious delusions. After a presumed seizure and fall, he develops delirium. What's causing these symptoms?



How would you handle this case?

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CASE Unresponsive after a presumed seizure

Mr. F, age 44, has schizophrenia. He is brought to the hospital by ambulance after he is found on the ground outside of his mother's house following a presumed seizure and fall. On arrival to the emergency department, he is unresponsive. His laboratory values are significant for a sodium level of 110 mEq/L (reference range: 135 to 145 mEq/L), indicating hyponatremia.

HISTORY Fixated on purity

Mr. F's mother reports that Mr. F had an unremarkable childhood. He was raised in a household with both parents and a younger sister. Mr. F did well academically and studied engineering and physics in college. There was no reported history of trauma or substance use.

During his senior year of college, Mr. F began experiencing paranoia, auditory hallucinations, and religious delusions. He required hospitalization and was diagnosed with schizophrenia. Following multiple hospitalizations over 5 years, he moved in with his mother, who was granted guardianship.

His mother said Mr. F's religious delusions were of purity and cleansing the soul. He spent hours memorizing the Bible and would go for days without eating but would drink large amounts of water. She said she

thought this was due to his desire to flush out imperfections.

In the past 3 years, Mr. F has been hospitalized several times for severe hyponatremia. At home, his mother attempted to restrict his water intake. However, Mr. F would still drink out of sinks and hoses. Mr. F's mother reports that over the past month he had become more isolated. He would spend entire days reading the Bible, and his water intake had further increased.

Prior medication trials for Mr. F included haloperidol, up to 10 mg twice per day; aripiprazole, up to 20 mg/d; and risperidone, up to 6 mg nightly. These had been effective, but Mr. F had difficulty with adherence. He did not receive a long-acting injectable (LAI) antipsychotic initially due to lack of access at the rural clinic where he was treated, and later due to his mother's preference for her son to receive oral medications. Prior to his current presentation, Mr. F's medication regimen was olanzapine, 10 mg twice a day; perphenazine, 8 mg twice a day; and long-acting

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Disclosures

The authors report no financial relationships with any companies whose products are mentioned in this article, or with manufacturers of competing products.

doi: 10.12788/cp.0167

Clinical Point

Low sodium levels could be due to psychotropics, psychiatrically-driven behaviors, or an underlying medical problem

propranolol, 60 mg/d. Mr. F had no other chronic medical problems.

EVALUATION Hyponatremia, but why?

Mr. F is intubated and admitted to the surgical service for stabilization due to injuries from his fall. He has fractures of his right sinus and bilateral nasal bones, which are managed nonoperatively. He is delirious, with waxing and waning attention, memory disturbances, and disorientation. His psychotropic medications are held.

Imaging of his head does not reveal acute abnormalities suggesting a malignant or paraneoplastic process, and there are no concerns for ongoing seizures. An infection workup is negative. His urine toxicology is negative and blood alcohol level is 0. His sodium normalizes after 3 days of IV fluids and fluid restriction. Therefore, further tests to differentiate the causes of hyponatremia, such as urine electrolytes and urine osmolality, are not pursued.

What could be the cause of Mr. F's hyponatremia?

- syndrome of inappropriate antidiuretic hormone
- diabetes insipidus due to antipsychotic use
- "beer potomania"
- psychogenic polydipsia

The authors' observations

The differential diagnosis for hyponatremia is broad in the setting of psychiatric illness. Low sodium levels could be due to psychotropic medications, psychiatrically-driven behaviors, or an underlying medical problem. Our differential diagnosis for Mr. F included iatrogenic syndrome of inappropriate antidiuretic hormone (SIADH), diabetes insipidus, or psychogenic polydipsia, a form of primary polydipsia. Other causes of primary polydipsia are related to substances, such as heavy beer intake or use of 3,4-methylenedioxymethamphetamine (MDMA, also known as "ecstasy"), or brain

lesions,¹ but these causes were less likely given Mr. F's negative urine toxicology and head imaging.

While psychogenic polydipsia is due to increased water consumption, both SIADH and diabetes insipidus are due to alterations in fluid homeostasis.^{2,3} *Table 12-4 (page 53)* outlines distinguishing characteristics of SIADH, diabetes insipidus, and psychogenic polydipsia. Urine studies were not pursued because Mr. F's sodium resolved and acute concerns, such as malignancy or infection, were ruled out. Mr. F's hyponatremia was presumed to be due to psychogenic polydipsia because of his increased fluid intake and normalization of sodium with hypertonic fluids and subsequent fluid restriction. During this time, he was managed on the surgical service; the plan was to pursue urine studies and possibly a fluid challenge if his hyponatremia persisted.

EVALUATION Delirium resolves, delusions persist

While Mr. F is on the surgical service, the treatment team focuses on stabilizing his sodium level and assessing for causes of altered mental status that led to his fall. Psychiatry is consulted for management of his agitation. Following the gradual correction of his sodium level and extubation, his sensorium improves. By hospital Day 5, Mr. F's delirium resolves.

During this time, Mr. F's disorganization and religious delusions become apparent. He spends much of his time reading his Bible. He has poor hygiene and limited engagement in activities of daily living. Due to his psychosis and inability to care for himself, Mr. F is transferred to the psychiatric unit with consent from his mother.

TREATMENT Olanzapine and fluid restriction

In the psychiatric unit, Mr. F is restarted on olanzapine, but not on perphenazine due to



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Table 1

Distinguishing characteristics of SIADH, diabetes insipidus, and psychogenic polydipsia

	SIADH ²	Diabetes insipidus ³	Psychogenic polydipsia ⁴	
Definition	Inappropriate secretion of ADH	Inability to concentrate urine	Compulsive water intake	
Cause(s)	Malignancies (lung, brain, paraneoplastic syndrome) Medications: SSRIs, TCAs, NSAIDs, anticonvulsants, and antipsychotics	Central diabetes insipidus Deficiency of ADH production or secretion due to trauma, genetics, and brain tumor	Nephrogenic diabetes insipidus Reduction in renal sensitivity to ADH due to medications, genetics, and obstruction	Malfunction of the hypothalamic-pituitary axis Compulsive behavior Dopamine receptor supersensitivity
Symptoms	None until severe hyponatremia (<120 mmol/liter)	Polydipsia, polyuria	Polydipsia, polyuria	
Laboratory findings	Serum sodium (mEq/L)	<135 (low)	>145 (normal to high)	<135 (low)
	Serum osmolality (mOsm/kg)	<275 (usually lower than urine osmolality)	>300 (high)	<275
	Urine osmolality (mOsm/kg)	>100	<300	<100
Diagnostics	Failure to correct sodium after normal saline infusion but correction with fluid deprivation	Central vs nephrogenic diabetes insipidus can be distinguished by vasopressin ^a administration	Urine osmolality will increase with fluid deprivation	
Treatments	Treat underlying condition, vasopressin antagonist (vaptan), loop diuretics, lithium, and demeclocycline	Central diabetes insipidus Desmopressin ^a	Nephrogenic diabetes insipidus Amiloride HCTZ	Clozapine, ACE inhibitors, opioid antagonists, and alpha adrenergic blockers may help. Behavioral therapy is mainstay of treatment

^aDesmopressin and vasopressin are synthetic analogues of ADH

ACE: angiotensin-converting enzyme; ADH: antidiuretic hormone; HCTZ: hydrochlorothiazide; NSAID: nonsteroidal anti-inflammatory drugs; SIADH: syndrome of inappropriate antidiuretic hormone; SSRIs: selective serotonin reuptake inhibitors; TCAs: tricyclic antidepressants

anticholinergic effects and not on propranolol due to continued orthostatic hypotension. Five days later, he is at his baseline level of functioning with residual psychosis. His fluid intake is restricted to <1.5 L per day and he is easily compliant.

Mr. F's mother is comfortable with his discharge home on a regimen of olanzapine, 25 mg/d, and the team discusses the fluid restrictions with her. The treatment team suggests initiating an LAI before Mr. F is discharged, but this is not pursued because his mother thinks he is doing well with the oral medication. She wants to monitor him with the medication changes in the clinic before pursuing an LAI; however, she is open to it in the future.

The authors' observations

Approximately 20% of patients with schizophrenia may experience psychogenic polydipsia.^{4,5} The cause of psychogenic polydipsia in patients with serious mental illness is multifactorial. It may stem from malfunction of the hypothalamic-pituitary axis, which leads to alterations in antidiuretic hormone secretion and function.^{4,6}

Mr. F's case highlights several challenges associated with treating psychogenic polydipsia in patients with serious mental illness. Antipsychotics with high dopamine affinity, such as risperidone and haloperidol, may increase the risk of psychogenic polydipsia, while antipsychotics

Table 2

Nonpsychiatric pharmacologic treatments for psychogenic polydipsia

Medication class	Hypothesized mechanism of action in psychogenic polydipsia
Angiotensin-II (AT-II) receptor blocker (irbesartan, losartan)	AT-II is a potent dipsogenic agent. It is hypothesized that dopamine may change AT-II's effect at the brain's AT-1 and AT-2 receptors, and chronic D2 blockade can cause polydipsia ¹¹
Opioid antagonists (naltrexone and naloxone)	The theory is that the continuous urge to drink water of psychogenic polydipsia is akin to addictive behaviors, which have shown positive response to blocking opioid receptors ⁹
Alpha-2-antagonist (mianserin)	Central adrenergic system is postulated to regulate drinking behavior via interactions with angiotensin II, acetylcholine, and beta-endorphin. Studies showed clonidine, a selective alpha-2 agonist, exacerbates polydipsia, and mianserin, an alpha-2 antagonist, relieves polydipsia ^{8,13}
Beta blockers (propranolol and pindolol)	Theory is based on the premise that AT-II is a potent dipsinogen. Beta blockers can inhibit renin release and thus indirectly inhibit AT-II. Another hypothesis is based on studies showing thirst is associated with increased norepinephrine in hypothalamic nuclei and evidence of increased CSF norepinephrine in patients with schizophrenia and psychogenic polydipsia ¹⁰
Demeclocycline	This tetracycline antibiotic inhibits adenylyl cyclase activation in the kidney. It is used to treat hyponatremia from syndrome of inappropriate antidiuretic hormone, and can induce nephrogenic diabetes insipidus ¹²

Clinical Point

Antipsychotics with high dopamine affinity may increase the risk of psychogenic polydipsia

with lower dopamine affinity, such as clozapine, may decrease the occurrence.⁵ Antipsychotics block postsynaptic dopamine receptors, which can induce supersensitivity by increasing presynaptic dopamine release in the hypothalamic areas, where thirst regulation occurs. This increase in dopamine leads to increased thirst drive and fluid intake.³

Quetiapine or clozapine may have been a better antipsychotic choice because these agents have lower D2 receptor affinity, whereas olanzapine has intermediate binding to D2 receptors.^{6,7} However, quetiapine and clozapine are more strongly associated with orthostasis, which was a concern during Mr. F's hospitalization. The weekly laboratory testing required with clozapine use would have been an unfeasible burden for Mr. F because he lived in a rural environment. Perphenazine was not continued due to higher D2 affinity and anticholinergic effects, which can increase thirst.⁶

In addition to switching to an antipsychotic with looser D2 binding, other

medications for treating polydipsia have been studied. It is hypothesized that the alpha-2 adrenergic system may play a role in thirst regulation. For example, mianserin, an alpha-2 antagonist, may decrease water intake. However, studies have been small and inconsistent.^{8,9} Propranolol,¹⁰ a beta adrenergic receptor blocker; irbesartan,¹¹ an angiotensin-II receptor blocker; demeclocycline,¹² a tetracycline that inhibits antidiuretic hormone action; and naltrexone,⁹ a mu opioid antagonist, have been studied with inconclusive results and a variety of adverse effects^{5,7,13} (Table 2⁸⁻¹³).

Behavioral interventions for patients with psychogenic polydipsia include fluid restriction, twice-daily weight checks, cognitive-behavioral therapy, and reinforcement schedules, which may be useful but less realistic due to need for increased supervision.^{11,12} Patient and family education on the signs of hyponatremia are important to prevent serious complications, such as those Mr. F experienced.

OUTCOME Repeated hospitalizations

Mr. F is discharged with follow-up in our psychiatry clinic and attends 1 appointment. At that time, his mother reports that Mr. F is compliant with his medication and has limited fluid intake. However, over the next 2 months, he is admitted to our psychiatric unit twice with similar presentations. Each time, the treatment team has extensive discussions with Mr. F's mother about strategies to limit his water intake and the possibility of residential placement due to his need for a higher level of care. Although she acknowledges that nursing home placement may be needed in the future, she is not ready to take this step.

Three months later, Mr. F returns to our hospital with severe abdominal pain and is found to have a perforated bowel obstruction. His sodium is within normal limits on presentation, and the psychiatry team is not involved during this hospitalization. Mr. F is treated for sepsis and undergoes 3 exploratory laparotomies with continued decline in his health. He dies during this hospitalization. The cause of Mr. F's perforated bowel obstruction is not determined, and his family does not pursue an autopsy.

The authors' observations

At Mr. F's final hospital presentation, his sodium was normal. It is possible Mr. F and his mother had found an acceptable fluid restriction routine, and he may have been doing better from a psychiatric perspective, but this will remain unknown.

Bottom Line

Patients with serious mental illness who present with hyponatremia should be evaluated for psychogenic polydipsia by assessing their dietary and fluid intakes, along with collateral from family. The use of antipsychotics with high dopamine affinity may increase the risk of psychogenic polydipsia. Behavioral interventions include fluid restriction, weight checks, cognitive-behavioral therapy, and reinforcement schedules.

Related Resources

- Sharp CS, Wilson MP. Hyponatremia. In: Nordstrom KD, Wilson MP, eds. Quick guide to psychiatric emergencies. Springer International Publishing; 2018:115-119. doi:10.1007/978-3-319-58260-3_21
- Sailer C, Winzeler B, Christ-Crain M. Primary polydipsia in the medical and psychiatric patient: characteristics, complications and therapy. *Swiss Med Wkly.* 2017;147:w14514. doi:10.4414/smw.2017.14514

Drug Brand Names

Amiloride • Midamor	Losartan • Cozaar
Aripiprazole • Abilify	Mianserin • Tolvon
Clonidine • Catapres	Naloxone • Narcan
Clozapine • Clozaril	Naltrexone • Revia
Demeclocycline • Declomycin	Olanzapine • Zyprexa
Desmopressin • DDAVP	Perphenazine • Trilafon
Haloperidol • Haldol	Propranolol • Inderal LA
Irbesartan • Avapro	Quetiapine • Seroquel
Lithium • Eskalith, Lithobid	Risperidone • Risperdal

This case highlights the clinical and ethical complexity of treating patients with psychogenic polydipsia. Because Mr. F no longer had autonomy, we had to determine if his mother was acting in his best interest as his guardian. Guardianship requirements and expectations vary by state. In our state of Missouri, a guardian is appointed by the court to act in the best interest of the ward, and may be a family member (preferred) or state-appointed. The guardian is responsible for providing the ward's care and is in charge of financial and medical decisions. In Missouri, the guardian must assure the ward resides in the "least restrictive setting reasonably available," which is the minimum necessary to provide the ward safe care and housing.¹⁴ Full guardianship, as in Mr. F's case, is different from limited

Clinical Point

Patient and family education on the signs of hyponatremia are important to prevent serious complications

Clinical Point

For psychogenic polydipsia, behavioral interventions include fluid restriction, weight checks, CBT, and reinforcement schedules

guardianship, which is an option in states such as Missouri. In limited guardianship, the court decides the extent of the guardian’s role in decisions for the ward.^{14,15}

Mr. F’s mother believed she was acting in her son’s best interest by having him home with his family. She believed by living at home, he would derive more enjoyment from life than living in a nursing home. By the time Mr. F presented to our hospital, he had been living with decompensated schizophrenia for years, so some level of psychosis was likely to persist, even with treatment. Given his increasingly frequent hospitalizations for hyponatremia due to increased water intake, more intense supervision may have been needed to maintain his safety, in line with nonmaleficence. The treatment team considered Mr. F’s best interest when discussing placement and worked to understand his mother’s preferences.

His mother continued to acknowledge the need for changes and adjustments at home. She was receptive to the need for fluid restriction and increased structure at home. Therefore, we felt she continued to be acting in his best interest, and his home would be the least restrictive setting for his care. If Mr. F had continued to require repeated hospitalizations and had not passed away, we would have pursued an ethics consult to discuss the need for nursing home placement and how to best approach this with Mr. F’s mother.

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