CLINICAL VIGNETTE

Hyponatremia Secondary to Non-Psychogenic Primary Polydipsia

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Abstract

Primary polydipsia can lead to hypotonic euvolemic hyponatremia, which is uncommon but can cause serious neurological symptoms. Primary polydipsia is often psychogenic in nature, but can also arise from iatrogenic causes, including the perceived need to increase fluid intake for health benefit. In this case, a 34-year-old male presented to the emergency department with worsening dizziness after starting emtricitabine/tenofovir for pre-exposure prophylaxis (PrEP). The patient's serum sodium and osmolality were low, as was urine osmolality, suggesting a primary cause of hypotonic hyponatremia. Free water restriction resolved the patient's symptoms within one day, and the patient was discharged with recommendation to stop PrEP and be careful to track and limit excessive free water intake. After discussing this unusual case of primary polydipsia, we review potential causes of euvolemic hyponatremia, including differentiating signs, symptoms, and laboratory tests, to put primary polydipsia in context and highlight the need to determine the history and perceptions about healthy fluid intake.

Introduction

Primary polydipsia is an important consideration in patients with hypotonic euvolemic hyponatremia. Though relatively uncommon, its effects can be serious, primarily consisting of neurologic symptoms such as headaches, dizziness, and confusion. However, primary polydipsia often presents alongside myriad other clinical conditions, meaning it may be difficult to identify. In the clinical literature, primary polydipsia is most commonly described in patients with chronic mental disorders and specifically identified as psychogenic polydipsia.[1,2] Classic causes of euvolemic hyponatremia include the syndrome of inappropriate antidiuretic hormone secretion (SIADH), thyroid or glucocorticoid deficiencies, and drug side effects.[3–5] Non-psychogenic, or iatrogenic, polydipsia can also occur, meaning this condition should be considered in patients even without other signs of psychiatric disease.[6] It can have diverse inciting events, but frequently includes patient misperceptions of the positive health impact of increasing fluid intake.[7–9] These cases can be especially complicated, since by definition they involve other, often vague, health complaints that the patient is using hydration to address. We report one such case of iatrogenic polydipsia, in which acute side effects of emtricitabine/tenofovir initiation for HIV pre-exposure prophylaxis (PrEP) led to prolonged increase in daily fluid intake. Dizziness related to pharmacotherapy led to increased fluid intake, which led to persistence of symptoms even after cessation of the medication.

Case Presentation

A 34-year-old male presented to the Emergency Room complaining of dizziness intermittently for the past 4 days. He had no significant past medical history. Alcohol intake averaged 5-10 drinks per week, with no other substance use. The patient started emtricitabine/tenofovir for PrEP three weeks prior to admission, and though he experienced some initial dizziness for two to three days after initiating PrEP, these symptoms resolved without intervention. Four days prior to admission, he experienced dizziness after a workout, which resolved after drinking water. Three days prior to admission, he experienced a second episode of dizziness and presented to an urgent care clinic. His serum sodium was 131 mmol/L and chloride was 95 mmol/L, prompting concern of dehydration and/or medication-associated side effects. On physician advice, the patient stopped taking emtricitabine/tenofovir and increased fluid intake.

Symptoms temporarily improved until the morning of admission, when the patient noted light-headedness. He had dramatically increased fluid intake, drinking a total of one gallon of water prior to admission, and presented to the Emergency Room for evaluation. He reported a frontal/bitemporal headache and intermittent tingling and numbness in his left hand. He denied other systemic symptoms, including nausea and vomiting, and denied recent alcohol or other substance use. He was on no other medications or supplements except for a protein powder supplement.

His vitals on admission were T 36.5 °C, BP 178/87, HR 69, RR 16, SpO_2 99% on room air. Serum sodium 125 mmol/L, potassium 3.6 mmol/L, and chloride 88 mmol/L. BUN 12 mg/dL, uric acid 4.7 mg/dL, and lactate 10 mg/dL. Serum osmolality was 257 mOsm/kg. Urine sodium was <20 mmol/L, osmolality was 78 mOsm/kg, pH 7.0, and specific gravity < 1.005. TSH was 1.5 mcIU/ml. EKG was unremarkable.

The patient was admitted to the internal medicine service and monitored for sodium correction on a regular diet. His creatinine clearance was followed throughout the admission and

remained above 89 mL/min based on the modified Cockcroft-Gault equation. His dizziness improved over 24 hours, and his serum sodium levels increased to 137 mmol/L and he was discharged the following morning.

Discussion

The underlying cause of hyponatremia can be challenging to identify because the condition can arise from a variety of very different sources. Understanding each of the important causes is important to develop a full differential, which can then be refined by a thorough history and targeted ordering of serum and urine laboratory studies.

When evaluating a patient with suspected hyponatremia, laboratory tests can be drawn both to assess the degree of sodium deficiency and the plasma osmolality, which may indicate a hypertonic, isotonic, or hypotonic state. Hypertonic and isotonic hyponatremias usually point to specific causative factors, such as hyperglycemia or hyperlipidemia.[3] In cases of hypotonic hyponatremia, the overall volume status of the patient must be clinically evaluated. Hypervolemia can generally be ruled out clinically, by noting absence of peripheral edema or ascites; but distinguishing between euvolemia and hypovolemia may be more challenging.[10] Euvolemic hyponatremia is, clinically, a diagnosis of exclusion, based on the absence of signs of hypovolemia such as dry mucous membranes, orthostatic hypotension, or decreased JVP.[3] Thus, some clinicians have recommended also assessing urine sodium output, with U_{Na} > 20-30 mmol/L generally indicating that the kidneys are receiving sufficient perfusion to exclude hypovolemia.[10] This measurement of urine sodium output, as well as overall urine osmolality, can then also be used to identify the most likely pathologic mechanism.

The most common cause of euvolemic hyponatremia is the syndrome of inappropriate antidiuretic hormone secretion (SIADH). In SIADH, U_{Na} is increased, generally >40 mmol/L, due to increased circulating levels of ADH, or vasopressin.[11] Increased water resorption from the kidneys leads to concentrated urine, and osmolality generally reaches >100 mmol/L.[3,12] Similarly, low levels of aldosterone and cortisol seen in adrenal insufficiency can lead to sodium and fluid loss, which can cause high urine osmolality when ADH increases in response.[13] Finally, hypothyroidism is associated with hyponatremia and a high urine osmolality as well, although the precise mechanism is not fully understood.[14] When urine osmolality is low or normal, the cause is generally low solute intake, as in beer potomania, which can be ascertained from a careful history or an increase in fluid intake, as is the case with primary polydipsia.[3]

Primary polydipsia can have myriad causes, but an important consideration is patient-driven fluid intake based on perceived medical benefit. Several cases secondary to medical advice have been reported, such as in preparation for procedures following advice to ”drink plenty”.[7,9,15] This patient’s recent initiation of PrEP may have contributed to increased water intake as well, as PrEP is known to cause dizziness in approximately 15% of patients, and the patient cited that symptom as a driver of his increased fluid intake.[16,17] Furthermore, there is some evidence for nephrotoxicity-induced polyuria and polydipsia following tenofovir administration.[18] Published reports estimate rates of nephrotoxicity in tenofovir at approximately 1%.[19] In addition to polyuria and polydipsia, this can manifest as glucosuria, proteinuria, hypophosphatemia, and hypokalemia. Associated free water intake can further exacerbate electrolyte disturbances, including hyponatremia, which leads to neurologic symptoms beginning at levels below 130 mmol/L.

The etiology of hyponatremia in primary polydipsia involves several interconnected mechanisms. First, increased free water intake dilutes existing blood sodium levels. This increases the need for kidneys to maximally dilute urine to excrete excess free water while minimizing solute loss. Although kidneys have a high capacity to excrete free water under normal circumstances, this requires regulation by antidiuretic hormone (ADH) to counteract the high osmotic gradient driving water out of the collecting ducts.[13] In cases of rapid high-volume water intake, as was seen in this patient, the kidney may maximally dilute urine (to 78 mOsm/kg in this patient) but still be unable to prevent solute loss to the degree required to prevent symptoms of hypotonic hyponatremia. Thus, the risk of hyponatremia in patients with primary polydipsia arises from rapid increased free water intake, but is modulated by kidney function, and thus assessing kidney function should be a key component of patient evaluation and management. The combination of laboratory studies, both serum and urine, and a full patient history can thus help to distinguish between hyponatremia driven by an underlying condition that may need further evaluation and treatment, and a primary cause such as polydipsia. Identifying the latter group of cases early can save patients from unnecessary tests and time in the hospital, and also reduce costs.

Conclusion

We describe a case of euvolemic hyponatremia in an adult male that first emerged with initiation of emtricitabine/tenofovir for pre-exposure prophylaxis and later reemerged due to primary polydipsia. The specific cause of euvolemic hyponatremia can be difficult to ascertain, partly because it can arise from multiple factors as was likely seen here, with possible contributions from both the drug regimen and a later case of polydipsia. Furthermore, while psychogenic polydipsia is a classic presentation of this condition, primary polydipsia can lead to very similar symptoms. In each case, a careful history can help to identify potential causes without the discomfort and expense of additional, in-depth laboratory testing. Increased awareness of the variable causes of euvolemic hyponatremia can thus reduce cost while enhancing effective patient care.

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