CLINICAL VIGNETTE

A Curious Case of Amlodipine Induced Hyponatremia

Jennifer Han, MD and Aarthi Arasu, MD

Case

A 70-year-old male with a past history of chronic hyponatremia, hypertension, hypothyroidism, obstructive sleep apnea, and atrial fibrillation presented to our endocrinology clinic for evaluation of chronic hyponatremia. Four years prior to our initial consultation, he was evaluated by endocrinology for acute symptomatic hyponatremia with episodes of fainting and profound weakness. Patient was subsequently admitted to an outside facility with a sodium level of 119 mmol/L. He was treated with normal saline intravenous fluid and was discharged with a sodium of 133 mmol/L. Review of laboratory examination showed that the sodium levels ranged from 125-138 mmol/L over the past four years. At our consultation, the patient reported persistent fatigue and dizziness but denied any polydipsia or polyuria.

The patient was on several antihypertensive medications including a valsartan/ hydrochlorothiazide combination pill, amlodipine besylate daily, and levothyroxine 25 mcg daily. Physical examination was unremarkable with normal blood pressure and pulse rate. Edema was not present on examination. Laboratory values taken at initial consultation showed a low sodium level of 125 mmol/L and Thyroid Stimulating Hormone of 3 mcIU/mL. Adrenal function, creatinine, urea, liver enzymes, bilirubin and glucose levels were within normal limits thereby excluding adrenal insufficiency, renal dysfunction, liver cirrhosis as possible causes of hyponatremia. Levothyroxine dose was increased to 50 mcg daily and hydrochlorothizide was discontinued. Initial laboratory data also showed hypoosmolar hyponatremia and patient had a euvolemic clinical status on physical examination and urine studies consistent with Syndrome of Inappropriate ADH secretion (SIADH).

The sodium level improved marginally to 128 mmol/L one month later and the patient was then started on a 1.5 liter fluid restriction. The sodium level initially improved to 132 mmol/L two months later but then later decreased down to 128 mmol/L five months post our initial consultation with recurrent symptoms of dizziness and fatigue. Amlodipine was discontinued and sodium levels increased to 135 mmol/L two weeks later and have remained higher than 135 mmol/L since that time.

Discussion

Hyponatremia is defined as a serum sodium concentration below 135mmol/L and is often discovered on a routine blood test.[1] Hyponatremia occurs in up to 8% of the population and up to 60% of hospitalized patients.[2] This is a common electrolyte disturbance that is associated with morbidity and mortality [3] and patients with even a mildly decreased sodium concentration have a 30% increased risk of death and have 14% longer hospitalizations than those with normal sodium levels.[2] Hyponatremia occurs secondary to changes in sodium and water status and represents a state of excess water relative to sodium.[4] The etiologies of hyponatremia are broad and include a variety of diseases and pharmacotherapy.[4] The presentation of hyponatremia range from brain edema with increased intracranial pressure and even brain herniation in the acute setting to changes in health associated with chronic hyponatremia such as osteoporosis, cognitive defects and fractures.[2]

The geriatric population represents a group that may be especially impaired by sodium levels. This subset of patients are more likely to experience hyponatremia secondary to multiple comorbid conditions, dehydration and polypharmacy.[4] Also challenging is the management of the geriatric population, as a clinical history may be difficult to obtain and unreliability of the physical examination assessment of volemic status and the multifactorial etiology of the electrolyte disorder.[4] Treatment of even mild hyponatremia appears to improve cognitive performance and balance in elderly patients.[4]

Drugs are a common cause of hyponatremia and hyponatremia is most commonly associated with diuretics, selective serotonin reuptake inhibitors and antiepileptics.[1] Most patients with drug induced hyponatremia are asymptomatic and mild cases can be treated by discontinuation of the offending agent or observation.[1] More severe cases of hyponatremia may require fluid restriction in addition to discontinuation of the medication.[1]

Amlodipine is a calcium channel blocker. The antihypertensive properties of calcium channel antagonists are caused mainly by a peripheral vasodilator effect but this class of medications also have natriuretic and diuretic characteristics.[5] Low doses of calcium antagonists can cause a marked increase in urinary sodium by up to four fold.[5] Another mechanism of hyponatremia may be via direct action on the renal tubulea with resultant increased sodium excretion and inhibition of renal

sodium reabsorption.[5] This natriuretic property seems to be common to all dihydropyridine calcium channel blockers and promotes their antihypertensive actions and which may be the mechanism of causing hyponatremia.

Calcium channel antagonist as a cause of hyponatremia is an extremely rare occurrence with perhaps one other case reported in the literature.[3] We report this case to remind providers to keep amlodipine in mind as a rare cause of drug induced hyponatremia and to especially consider this medication as a cause of chronic hyponatremia in the elderly population.

REFERENCES

1. **Fourlanos S, Greenberg P.** Managing drug-induced hyponatraemia in adults. *Aust Prescr.* 2003;26:114-730 Sep 2003DOI: 10.18773/austprescr.2003.083
2. **Nagler EV, Vanmassenhove J, van der Veer SN, Nistor I, Van Biesen W, Webster AC, Vanholder R.** Diagnosis and treatment of hyponatremia: a systematic review of clinical practice guidelines and consensus statements. *BMC Med.* 2014 Dec 11;12:1. doi: 10.1186/s12916-014-0231-1. Review. PubMed PMID: 25539784; PubMed Central PMCID: PMC4276109.
3. **Liamis G, Milionis H, Elisaf M.** A review of drug-induced hyponatremia. *Am J Kidney Dis.* 2008 Jul;52(1):144-53. doi: 10.1053/j.ajkd.2008.03.004. Epub 2008 May 12. Review. PubMed PMID: 18468754.
4. **Soiza RL, Cumming K, Clarke JM, Wood KM, Myint PK.** Hyponatremia: Special Considerations in Older Patients. *J Clin Med.* 2014 Aug 18;3(3):944-58. doi: 10.3390/jcm3030944. Review. PubMed PMID: 26237487; PubMed Central PMCID: PMC4449639.
5. **Malaterre HR, Kallee K, Daver LM.** Hyponatremia and amlodipine therapy. *Cardiovasc Drugs Ther.* 1999 Apr;13(2):171-2. PubMed PMID: 10372233.

Submitted September 21, 2017