Hyponatremia Induced by Amiodarone Therapy

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The syndrome of inappropriate antidiuretic hormone secretion, known as SIADH and first reported by Bartter and Schwartz in 1967 [1], is the most common cause of euvolemic hyponatremia. It is due to non-physiological release of arginine vasopressin from the posterior pituitary. Hyponatremia induced by SIADH can be caused by several conditions, including central nervous system disorders, malignancies, various non-malignant lung diseases, hypoadrenalism and hypothyroidism, as well as various drugs. Amiodarone is an effective anti-arrhythmic agent for life-threatening arrhythmias but has some non-cardiac toxicity. SIADH induced by amiodarone during long-term therapy appears to be a rare adverse effect. We report a case of hyponatremia associated with add-on therapy of amiodarone, and discuss its clinical implications.

Patient Description

An 85 year old man was admitted due to chest pain, abdominal pain and weakness. His medical history included coronary artery disease: one month prior to admission he underwent percutaneous transluminal coronary angioplasty and began to receive treatment with amiodarone for recurrent arrhythmia (atrial fibrillation) that appeared shortly after this procedure. In addition, he had hypertension, hyperlipidemia, peripheral vascular disease, chronic renal failure, hypothyroidism, and benign prostatic hypertension. Laboratory tests on admission were normal, except for a sodium level of 122 mEq/L accompanied by non-specific symptoms of weakness, dizziness, abdominal pain and symptomatic bradycardia. Blood osmolarity was 261 mOSM, uric acid 6.5 mg/dl, urine electrolytes were sodium 33 mEq/L and potassium 85 mEq/L, and urine osmolarity was 291 mOSM. Since no recent changes had been made in any of his drugs (amlodipine, enalapril, isosorbide mononitrate, thyroxine, acetylsalicylate, clopidogrel, simvastatin, alfuzosin, omeprazole), and other medical conditions associated with hyponatremia (infections, tumors) were unlikely, we speculated that his new-onset hyponatremia, whose laboratory features supported the diagnosis of SIADH, was secondary to the recent therapy with amiodarone. Of note is that the patient's hypothyroidism was adequately treated. Following cessation of amiodarone therapy, his sodium levels normalized within a few days and remained so at a follow-up visit 3 months later.

Comment

Amiodarone can cause hyponatremia, most probably due to a SIADH-induced mechanism. Although this phenomenon occurs only rarely, it should be recognized by clinicians as a possible serious adverse effect of this drug. The mechanism of SIADH-induced hyponatremia secondary to amiodarone is unclear. Most drugs that cause SIADH do so by sensitizing the kidneys to antidiuretic hormone, stimulating release of antidiuretic hormone, or both. We speculate that amiodarone might induce SIADH by its channel-modulating properties on renal or neural tissues. Since severe hyponatremia can produce significant neurological damage and is associated with a high mortality rate, clinicians should be aware that this complication may occur during amiodarone therapy, and they should suspect hyponatremia once non-specific symptoms are reported by their patients. As already mentioned, a few similar cases were reported previously. In one report an elderly woman presented with significant hyponatremia caused by SIADH during therapy with amiodarone. The hyponatremia resolved after discontinuation of the drug and did not recur during a follow-up of 6 months [2]. In another case a 67 year old man developed hyponatremia consistent with SIADH. Amiodarone was discontinued and the patient's serum sodium level began to rise within 3 days of discontinuation and returned to normal within 1 month [3]. These two cases are similar to ours in that the hyponatremia quickly resolved after cessation of amiodarone use. Another clinical report described two elderly patients who developed hyponatremia caused by SIADH that occurred during the initial loading period of amiodarone therapy. Both patients recovered within 3 weeks after reduction of the dose, even though amiodarone was continued [4]. In that report, as compared to our patient, the drug was not discontinued but the hyponatremia was resolved after dosage reduction. It is noteworthy that SIADH has also been reported in association with other anti-arrhythmic drugs such as lorcainide and propafenone.

In conclusion, we present a case of amiodarone-induced hyponatremia. This presumably rare phenomenon should be considered in patients treated with amiodarone, mainly during the first weeks of therapy. Amiodarone-induced SIADH may develop during the loading phase [5], but whether cessation of treatment or only dose reduction is an appropriate

SIADH = syndrome of inappropriate antidiuretic hormone

response to this hyponatremia is yet to be determined.

References

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