Biomedicine: 2024; 44(2):240-242 *April-June 2024*
Case Report

Selective Serotonin Reuptake Inhibitor Associated Syndrome of Inappropriate Antidiuretic Hormone Secretion: A Case Report

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(Received : 04.05.2024 Revised : 19.06.2024 Accepted : 11.07.2024)

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ABSTRACT

A sixty-year-old female was brought to the emergency for acute confusion. She was on treatment for hypertension and depression. The general physical examination and neurological examination were normal except for mild hypertonia. The immediate non-contrast computed tomography was unremarkable. However, her blood investigations revealed severe hyponatremia. On further evaluation, she was considered to have the syndrome of inappropriate antidiuretic hormone secretion (SIADH). The patient had been taking sertraline for the past six months. In the absence of any other explanation, sertraline was attributed to be the cause of SIADH. Sertraline is a selective serotonin reuptake inhibitor (SSRI). Though SSRIs are considered to selectively inhibit reuptake of serotonin, they also inhibit reuptake of noradrenaline as well. Noradrenaline can stimulate the release of ADH through alpha one receptor. The patient was treated with hypertonic saline with close monitoring of serum sodium level. As the serum sodium level increased, the patient's sensorium gradually improved. Sertraline was discontinued and the patient was discharged with antihypertensives. On subsequent follow-up, she remained stable and asymptomatic.

Key words : Sertraline, euvolemic hyponatremia, SIADH

Introduction

SIADH (syndrome of inappropriate antidiuretic hormone secretion) can be defined as excessive production of ADH in absence of an adequate physiological stimulus. Malignancy, infection medications are some of the common causes of SIADH (1,2). It usually manifests as hyponatremia and the symptoms of SIADH are attributed to hyponatremia. An elderly female had presented with an acute confusional state. On investigation she was found to have severe hyponatremia (serum sodium level 115mEq/L). Acute severe hyponatremia can manifest as acute confusion, delirium, seizure, coma etc. due to cerebral oedema. She was successfully managed with 3% hypertonic saline. Her hyponatremia was considered to be due to SIADH as she fulfilled the clinical criteria formulated by Schwarz and Bartter (2,3). After ruling out other possibilities SIADH was attributed to be due to Sertraline which the patient was taking for her depression. Sertraline was discontinued and the patient was subsequently discharged in stable condition.

Case Report

Presentation - A 60-year-old female, known case of hypertension for ten years and depression for six months was brought to the emergency with a history of acute confusional state since last ten hours. There was no history of loss of consciousness, seizures, fever, headache, or vomiting. On presentation, pulse rate was 72 beats per minute, blood pressure was 160/90 mm of mercury, respiratory rate was 24 per minute, and the patient was afebrile., and oxygen saturation was 96% in room air. There were no peripheral signs of dehydration. Pupils were bilaterally normal-sized and reactive. Central nervous system examination revealed normal cranial nerves, mildly increased muscle tone bilaterally, power 5/5 bilaterally, normal deep tendon reflexes, and

bilateral flexor plantar response with intact cerebellar signs. The rest of the physical examination did not reveal any abnormality. She was taking tablets of telmisartan and metoprolol for her hypertension. She was on sertraline 50mg daily for her depression.

Investigation-A non-contrast CT head was done, which showed mild cerebral atrophy. ECG showed normal sinus rhythm. Random blood sugar was 143 mg per deciliter. Her hemogram was normal with a total leukocyte count of 7600/cubic mm. Blood urea was 24mg% and serum creatinine were 0.9mg%. The liver function test was normal Serum electrolytes revealed hyponatremia with a serum sodium level of 115 mEq/(135-145mEq/L). Further, the patient was worked up for the cause of hyponatremia. The urine sodium level was 101 mEq/L. Serum osmolality was 234 mOsm/L. Urine osmolality was 260.4 mOsm/kg. The thyroid profile was within normal limits. There was no evidence of adrenal insufficiency, cardiac failure, renal disease, or hepatic dysfunction. SIADH was diagnosed according to the Schwartz and Bartter criteria.

Management- As the hyponatremia was acute onset, the patient was treated with 3% sodium chloride solution and serial serum sodium level monitoring. Serum sodium was monitored to raise the level not more than eight mEq/L in 24 hours to avoid the risk of osmotic demyelination. Subsequently, the patient improved symptomatically and experienced complete cognitive recovery. As septicemia was unlikely no antibiotic was prescribed.

Further on, the patient was evaluated for the cause of SIADH. After ruling out other causes based on detailed history, examination, imaging, and laboratory workup, the drug sertraline was deemed to be the cause of SIADH. The patient and relatives were counselled regarding discontinuation of Sertraline. They were further reassured to start other medication for depression on follow up if required. The patient was discharged in a clinically stable condition. Follow-up for a period of 9 months revealed no further hyponatremia and had not required any antidepressant.

Discussion

Hyponatremia, due to SIADH, is a rare side effect of SSRIs like sertraline. ADH acts on the renal tubules to reduce water loss and concentrate the urine. Excessive or inappropriate ADH production impairs urinary water excretion and predisposes to hyponatremia if water intake is not reduced in parallel with urine output1. Symptoms of SIADH are lethargy, headache, insomnia, nervousness, apathy, agitation, confusion, convulsion, and coma (2). If hyponatremia develops gradually or has been present for more than a few days, it may be largely asymptomatic. Schwarz and Bartter formulated a clinical criterion for the diagnosis of SIADH in 1967, which is valid till today (2,3). It is characterized by a serum sodium level less than 135 mEq/L, serum osmolality less than 275 mOsm/kg, urine sodium greater than 40 mEq/L, urine osmolality greater than 100 mOsm/kg, the absence of clinical evidence of volume depletion, and the absence of other causes of hyponatremia.

Our patient fulfilled these criteria, and hence, a diagnosis of SIADH was reached. Further workup pointed towards the intake of the drug sertraline, an SSRI, as the cause of this SIADH. Selective serotonin reuptake inhibitors affect the levels of the neurotransmitter norepinephrine. Under normal physiology, norepinephrine stimulates the alpha-one adrenergic receptor, leading to ADH release. Subsequently, norepinephrine is degraded, and the stimulatory signal on ADH release gets terminated. During SSRIs use, the reuptake of norepinephrine is inhibited, and the stimulatory signal continues to act. This leads to increased release of ADH. (4) There is a threefold increased risk of developing SIADH with SSRI use than with other antidepressants (5). The incidence of hyponatremia associated with SSRI varies from 0.5% - 32 %. Risk factors for the development of hyponatremia with SSRI use include older age, female gender, concomitant use of diuretics, low body weight and low baseline serum sodium (6).

The mainstay of treatment of SIADH is correction of hyponatremia and treatment of the underlying cause. In case of acute severe hyponatremia, 3% hypertonic saline infusion is the treatment of choice. However, serum sodium level should be closely monitored. To avoid osmotic demyelination syndrome serum sodium level should not be raised by more than 6 to 8 mEq/L/24 hours. Fluid restriction, salt administration and vasopressin receptor antagonists are other modes of treatment. Salt in the form of tablet or capsule may be given with loop diuretics. Vasopressin receptor antagonists like tolvaptan should be avoided in liver disease. In case of adrenal insufficiency corticosteroid replacement is required. The short-term prognosis of SIADH depends on the early diagnosis and correction of hyponatremia. The long-term prognosis is dependent on diagnosing and managing the underlying cause.

Conclusion

Sertraline is a commonly prescribed drug and cognitive impairment like confusion may get ignored in the backdrop of depression. So, it is particularly important that physicians should be aware of such situations so that the patients can be managed at the earliest. The exact mechanism of hyponatremia due to SSRIs is not known, however experimental studies have shown that noradrenaline and dopamine reuptake are also inhibited. Further studies are required to elucidate the underlying pathophysiology. SSRIs and other antidepressants should be carefully prescribed in the elderly. Patients on these medications should be periodically reviewed for consideration of deprescribing or discontinuing them. While patients are on such medications, the occurrence of new symptoms should raise an alarm and the possibility of development of SIADH should be considered. Serum electrolyte level monitoring is advisable in such cases.

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Informed Consent- Written consent has been obtained from the patient (after her recovery) and her husband.

Acknowledgment

We are thankful to the patient for the opportunity to enhance our knowledge.

Source of funding – Nil

Conflict of interest - None