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SIADH: A RARE ENTITY IN HEAD AND NECK CANCER- A CASE REPORT WITH REVIEW OF LITERATURE

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ABSTRACT Hyponatremia secondary to malignancy is a rare finding. Syndrome of inappropriate ADH secretion in head and neck cancer patient can be a serious comorbidity leading to decline in the survival rate. However, most of the time it goes undetected at the outset. And the pathophysiology of this link is not clarified. This article highlights a case of SIADH developed in 40-yr-old man with oral cancer. Also, focusses on the importance of diagnosing it and rendering treatment at the earliest.

KEYWORDS : hyponatremia, ADH, squamous cell carcinoma, SIADH, metabolic disorder

INTRODUCTION

Syndrome of inappropriate antidiuretic hormone secretion is the disease characterized by loss of sodium through urine due to hypersecretion of antidiuretic hormone. The occurrence of this is often reported as a systemic response to cancer defined by a serum sodium level <135 mEq/L [1]. Around 67% cases reported in the literature are related to small cell carcinoma of the lung [2]. Decrease in plasma sodium concentration being a common finding in hospitalized patients, hyponatremia is not given much clinical significance [3]. The euvolemic state of extracellular fluid has to be ascertained before confirming SIADH as it remains a diagnosis of exclusion. However, it goes undetected in the early phase due to the physiological compensation. Here, we report a case of oral cancer found to have SIADH.

Case Report

A 40-year old male patient sorted the out-patient department on 19th august 2016 with two months history of painful growth over left inner cheek region and weight loss since 6 months. He also had a history of chronic tobacco chewing and alcohol consumption. He did not have any significant medical history. Further, eliciting the details and evaluating the patient, imaging and routine laboratory investigations were done. Electrolyte panel showed mild decrease in the value of sodium, not very significant. Followed by this, biopsy was performed which revealed well differentiated squamous cell carcinoma of left buccal mucosa and gingivobuccal sulcus. Patient underwent surgery for the same on 22nd September 2016. And, the Immediate post-operative days were uneventful.

As per the protocol followed by the unit, a complete hemogram and electrolytes were repeated on 5th post-operative day, which showed serum sodium level of 123.4mmol/L without any symptoms of hyponatremia. Based on this, a repeat investigation was done for confirmation, which again revealed a decreased level.

Considering the hyponatremia, sodium correction was performed in accordance with the protocol. Subsequent investigation did not show any improvement. On 10th post-operative day patient developed delirium with a GCS score of E3V3M5. Following this renal, liver and thyroid function test were done to rule out the causes of pseudo hyponatremia and all were within normal limits. Few more laboratory investigations were done with the results including a serum sodium 120 mmol/L and serum osmolality 256 mOsm/kg. The urinary osmolality was 324 mOsm/kg and urinary sodium 122 mmol/L. Also, plasma AVP levels were inappropriately elevated relative to plasma Osmolality.

After differentiating from the other causes of hyponatremia SIADH was diagnosed based on the relevant findings. The patient was treated with 3% hypertonic saline infusion, oral salt supplement and fluid restriction. By 14th post-operative day symptoms subsided and the values were normalized. The GCS score improved to E4V5M6.

The etiology of SIADH here could be ectopic production of ADH by tumour itself. The symptoms subsided within few days of treatment, electrolyte values were normalized and the patient recovered.

DISCUSSION

Alexander Leaf and Audley R. Mamby initially described SIADH in the year of 1951 [4]. Later, Schwartz in 1957 was the first to suggest that small cell carcinoma produced some quantity of antidiuretic hormone [2]. He described hyponatremia associated with urinary sodium loss in two patients with lung cancer [5]. Hypothesis proposed by Schwartz was proven by detecting ectopic AVP in small cell carcinoma of the lung with inappropriate diuresis [6]. Early identification of the cause and precise treatment is required for normalization of the same.

The incidence of SIADH is about 3% in head and neck cancer [7,8]. It was Moses et al. in 1976 who first described SIADH in patients with squamous cell carcinoma [9]. Head and neck malignancy linked with SIADH is mostly found in oral cavity although various other sites are reported [10].

In 1987 Tadashi okotumo et al reported a case of SIADH

caused by ectopic production of arginine vasopressin (AVP) by squamous cell carcinoma of tongue and floor of mouth [11]. Zohar et al in 1991 described four patients with advanced cancer of the head and neck region with coexisting SIADH [12]. Similarly, in 2005 Danielides et al reported a case secondary to recurrent oral cancer [13].

Most of the patients remain asymptomatic initially followed by symptoms like nausea, tremors, depression, hallucination and lethargy to severe neurological manifestations [7]. The earliest findings noted are nausea and malaise when the plasma sodium concentration falls below 125 mEq/L to 130 mEq/L. And severe neurological manifestations are seen when it falls abruptly below 115 mEq/L to 120 mEq/L [14]. The symptoms may precede or accompany diagnosis or intervention for the tumor and may be detected only in few patients[15].

It is also important to exclude adrenal insufficiency and hypothyroidism before concluding SIADH secondary to malignancy. As former elevates plasma ADH and latter causes impaired diluting ability[16,17].

The main determinant of plasma osmolality is the sodium concentration. When plasma osmolality decreases, water shift from the extracellular to the intracellular fluid compartment leading to hyponatremia. The neurologic symptoms that may be associated with hyponatremia is further due to overhydration of brain cells[18]. Although the serum sodium levels decrease progressively, due to the brain's adaptive mechanisms symptoms doesn't appear in the early phase. Further failure of adaptation leads to the appearance of mild to severe neurological symptoms[19]. The key to effective management is timely diagnosis and strategic treatment planning.

Schwartz and Bartter in 1967 defined diagnostic criteria for SIADH which excludes other systemic causes. (Table 1)[5].

Schwartz and Bartter Criteria
• Serum sodium <135mEq/L
• Serum osmolality < 275 mOsm/kg
• Urine sodium > 40 mEq/L
• Urine osmolality >100 mOsm/kg
• Absence of clinical evidence of volume depletion
• Absence of other causes of hyponatremia
• Correction of hyponatremia by fluid restriction
Additional Criteria
• Serum uric acid <4mg/dl
• Worsening of hyponatremia with IV normal saline infusion
• Plasma vasopressin elevated relative to serum osmolality
• Abnormal response to water load test

After establishing the diagnosis, adopting the right treatment protocol matters for the faster resolution of the condition. According to Moses et al. fluid restriction to about 800-1000 ml daily is required to treat mild to moderate symptoms. It can lead to steady increase in serum sodium or osmolality [9]. Similarly, according to Onitilo et al fluid restriction around 500 ml/day to 1000 ml/day may be useful for treating mild asymptomatic hyponatremia [20]. And severe cases should be treated with 3% hypertonic saline to increase free water excretion under close monitoring.

Rapid correction in asymptomatic patients may lead to a fatal neurological condition called osmotic demyelination syndrome which may be due to sudden loss of tonicity of neural cells. Therefore, in asymptomatic patients, sodium correction should not be done more than 8 mmol/L/24 hours whereas in symptomatic patients, not more than 10 mmol/L/24 hours to 12 mmol/L/24 hours [21]. The case we described here was treated with fluid restriction to 1000ml/day and hypertonic saline infusion for sodium correction with very close monitoring of serum sodium levels in the initial 24-48 hours. Symptoms resolved within few days of initiation of the treatment.

Negative fluid balance leading to the normalized serum sodium level by method of fluid restriction is the mainstay of the treatment. Presently, there are drugs antagonizing the vasopressin type 2 receptor in the distal tubule aiming highly effective treatment, advantage being correction without any discomfort of fluid restriction [22]. But, according to literature focus should be majorly on treating the etiology, that is the malignancy itself. The algorithm we adopted included removal of the cause along with systematic treatment in accordance with the criterion.

CONCLUSION

Detailed clinical history with adequate laboratory investigations direct towards accurate diagnosis which is critical to ensure appropriate therapy. The studies conducted so far proves SIADH can have deleterious effect in patients with malignancy especially in terms of survival as it is a serious comorbidity. Early identification and treatment of the underlying etiology is crucial to eliminate the root cause of SIADH. However, it is also important to have additional studies enlightening the pathophysiology of SIADH secondary to malignancy.

Abbreviations:

SIADH : Syndrome Of Inappropriate Antidiuretic Hormone Secretion, GCS: Glasgow Coma Scale, ADH: Antudiuretic Hormone

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