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CASE REPORT

IN THE DEEP SEA OF HYPONATREMIA: A CASE SERIES

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Abstract:

Hyponatremia is a matter of concern in clinical practice. Hyponatremia can be associated both low or high tonicity and even with normal tonicity. Although severity and morbidity varies widely but sometimes serious hazard can occur from misdiagnosis or late diagnosis. In these 3 case we will discuss different pattern of presentations of hyponatremia. Megestrol acetate is a synthetic progestin used to treat the symptoms of loss of appetite and wasting syndrome in people with AIDS-related cachexia, breast cancer or endometrial cancer. Herein, we report a case of 32 years' female presented with clinical and biochemical features of central adrenal insufficiency who was taking megestrol acetate chronically. Pituitary function was otherwise essentially normal. Another case about a 46 year old male who was getting treatment for schizophrenia and later found to have hypopituitarism. Our last case about a male of 35 years old who was also diagnosed to have pituitary insufficiency

Key words: *Hyponatremia, Pituitary insufficiency, Megestrol acetate, Adrenal insufficiency, ACTH suppression.*

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Introduction:

Hyponatremia is most frequently found electrolyte imbalance among the hospitalized patient[1]. When Sodium Concentration in the blood came below 135 mmol/l it is defined as hyponatremia[1]. Dilutional hyponatremia is more common among the different classes of hyponatremia which is caused by water retention and promotes life threatening complications[2]. Among other the nonhypotonic hyponatremias are hypertonic hyponatremia, isotonic hyponatremia, and pseudohyponatremia[3].

The common causes of hyponatremia are due to renal sodium loss by use diuretic agents, adrenal insufficiency and by excessive sodium loss due to diarrhea, vomiting, congestive cardiac failure, renal failure, burns, primary polydipsia, SIADH[4,5]. When Sodium level is low it is unwise to only give treatment without finding the underlying cause. Sometimes even after searching cause could not be found. An approach to the diagnosis of hyponatremia needs conscious and sincere history taking including drug history, meticulous clinical examination of cardiac, pulmonary,

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renal, neurological system[13]. Along with all routine clinical investigations urine osmolarity, plasma osmolarity and 24hour urinary Sodium measurements is pivotal for diagnosis[13]. For the complete evaluation of hyponatremia imaging of brain, hormonal and hypothalamo-pituitary-adrenal axis is sometimes necessary[14].

Case reports:

Case 1:

A 32 years old normotensive, non-diabetic female admitted in hospital with the complaints of persistent vomiting for three months. Vomiting was non projectile that occurred 5-7 times daily. Vomitus contained clear watery liquid, which was mild to moderate in amount. There was no undigested food particles, it was neither bile stained nor blood mixed. It was not associated with abdominal pain, headache but she complained about anorexia. She also gave a history of recent 15 kg weight loss which was unintentional.

She gave history of taking different antibiotics, antiemetic for her illness. On examination, The patient was afebrile, with a blood pressure of 100/70 mmHg on sitting position which was 80/60 mmHg in standing position. She appeared restless, toxic, her mucous membranes were dry and there was poor skin turgor. Inspection of abdomen revealed mildly distended abdomen with wide striae's which were purple colored, more on peripherally. She was fully oriented and cardiac, pulmonary & musculoskeletal examination were unremarkable and there were no gross neurologic deficits. Abnormalities on the blood chemistry panel included a low sodium of 122 mmol/L (normal range, 136–145), potassium of 4.96 mmol/L (normal range, 3.5–5.10), low bi-carbonate of 19 mmol/L (normal range, 22-28), hemoglobin of 15.4 g/dL (normal range, 12-14.5), HCT of 48.20% (normal range-34-45), RBS 6 mmol/l. Urine RME revealed mild albuminuria, plenty of pus cell with severe ketonuria.

On further questioning her drug history revealed that ,10 months back she had taken 1800 mg megestrol acetate daily for about 3 months to improve her anorexia which was developed after death of her first child. The patient's last menstrual period 1 month back which was regular. She denied galactorrhea, headaches or vision changes. There was no family history of pituitary or adrenal gland disease and there was no hyper-pigmentation of the palmar creases or buccal mucosa. As the diagnoses considered by the admitting team was adrenal insufficiency, and a serum cortisol & ACTH level was drawn at 8:00 am the next morning. When the result returned at 0.88 mcg/dL &<1.00 pg/mL respectively, short synacthen test was performed at 8.00 am of next morning, which concluded central adrenal insufficiency. Results of Short Synacthen test came positive for adrenal insufficiency. Other pituitary hormones were normal.

Oral hydrocortisone was started at a dose of 20 mg at morning and 10 mg at afternoon.

Within 24 hours, the patients' symptoms had improved and she appeared much more energetic; hydrocortisone was continued. The endocrine laboratory results are shown inTable 1. A magnetic resonance imaging (MRI) scan of brain with and without gadolinium revealed normal pituitary gland.

Case 2:

Mr Y, 46years old, normotensive, non diabetic, non asthmatic, non smoker and non alcoholic man got admitted to PMCH with the complaints of vomiting for 5 days . Vomiting was non projectile that occurred 5-7 times daily. Vomitus contained clear watery liquid, which was mild to moderate in amount. There was no undigested food particles, it was neither bile stained nor blood mixed. It was not foul smelling and not preceded by nausea. It was not associated with abdominal pain, loose motion, headache, blurring of vision, dizziness, vertigo, chest pain, fever. The patient had a history of recurrent episode of similar pattern of vomiting for several times in the last 18 years. About 18 years back when he was at Middle East he had his first episode of vomiting. That time after few days he started to talk irrelevantly with gradual development of disorientation. For this problem he was admitted to the nearby local hospital, then he was sent to Bangladesh after recovery. He failed to recall this incident in exact manner. In around 2005 ,along with vomiting he developed low mood, started to remain home all the time and avoided social gathering. After some days, he developed incoherent talks with violent behavior. With these problems, he got admitted to a private hospital in Dhaka, where he had been diagnosed as a case of schizoaffective mood disorder and was under psychiatric evaluation. When conditions still did not impropve, he was consulted by a neurologist for better evaluation. Here, he had been diagnosed as a case of paranoid schizophrenia with recurrent hyponatremia due to salt-losing nephropathy. Fludrocortisone was added on his treatment. After receiving infusions and injections, his condition improved slightly but then again, the situation of his recurrent vomiting and immediate hospital admission repeated again and again. In addition to all these, he had a lower sexual drive due to decreased libido and erectile dysfunction. For further evaluation and treatment, he got admitted to PMCH on 30th Octobor 2021. On general examination, he

was apathetic, mildly anemic, non-icteric, with body built below average. His decubitus was on choice. He had no visible pigmentation. He had loss of hair in axillary area. His pulse was 76 beats per minute, blood pressure was 110/70mmHg in sitting position and 90/60mmHg in standing position. Examination of other systems revealed no abnormalities.

His investigations revealed severe hyponatremia (116 mmol/l), 24 hour urinary electrolytes within normal limit. Urine osmolality 212 mosm/kg, Plasma Osmolality 227 mosm/kg.MRI revealed Partial empty sella. No other significant abnormality in MRI Brain. Baseline cortisol found to be 0.76 mcg/dl (Normal range: 4.458-22.689 mcg/dl), ACTH 11 (7.2-63.98 pg/ml) and short synacthen test cortisol was 42.51 nmol/l (Normal: >690 nmol/l). LH 1.12 mIU/ml (2.0-12.0 mIU/ml), Testesterone 9.08 (Normal: 10.40-35.71 nmol/l).

After investigations he was diagnosed to have hypopituitarism.

Case 3:

Mr. Abdul Wadud, 35 years old normotensive, non-diabetic, non-smoker, non-alcoholic man admitted to PMCH with the complaints of vomiting for 10 days. According to the patient's statement, while he was in Oman he developed fever 12 days back. It was high grade, intermittent in nature, persisted for 2 days, not associated with chills and rigors, subsided after taking paracetamol and highest recorded temperature was 103°F.After 2 days, he developed vomiting, 3-4 times daily, projectile in nature, not preceded by nausea, occurred mainly after eating, contained undigested food particle. It was neither bile nor blood stained & wasn't foul smelling. At 3rd day of vomiting patient suddenly became unconscious & he got admitted at hospital in Oman. Unconsciousness was not associated with any episode of seizure, no frothy discharge from mouth, no H/O fall or trauma or any weakness of any specific side of the body. Within 2-3 hour of admission; he regained consciousness after receiving infusions and some injections. There was no confusion after regaining his sense. He stayed in the hospital for 2 days. With treatment, the frequency of vomiting decreased and he was discharged from hospital in 3rd November. Then he came back to Bangladesh on 6th November, 2021. He again developed vomiting in similar manner. For further evaluation he got admitted in PMCH on 8th November. There was no H/O abdominal pain, yellow coloration of skin, sclera or urine, cough, hematemesis, malena, headache, vertigo, chest pain, skin rash, swelling, voice change, palpitation, blurring of vision.

On query he said he had history of 4 kg weight loss in last two months which was unintentional and associated with anorexia. It was not associated with palpitation. He also stated that he felt extremely lethargic and sleepy for the most of the time in day for last 2 months. He also stated about developing intolerance to cold. On query he mentioned that he had decrease frequency of shaving for last 6 months. He also complained about less sexual drive in last 7 years but now the problem is increasing.

On general examination he was irritated, mildly anemic, non-icteric, with average body build. He has pigmentation over the nose & cheek. He has loss of hair in axillary & pubic area. His Bp was 110/80 mm of hg in sitting position & 90/70 mmhg in standing position. Examination of other systems revealed no abnormality.

His investigations revealed Severe Hyponatremia (108 mmol/l), Blood count, RBS was normal. MRI of Pituitary was also normal. His baseline cortisol was low 0.84(Normal range: 4.45-22.68 mcg/dl), ACTH 13.38(Normal range: 7.2-63.38 pg/ml), LH <0.2 (2-12 MIU/ml), FSH 0.32 mIU/ml(Normal range: 1.0-8.0 mIU/ml), in Short synacthen after 1 hour cortisol level were still below normal level 2.97 microgram/dl.

He was diagnosed to have hypopituitarism although the cause could not be evaluated because of economical limitations.

Discussion:

Recognizing the presentation of hyponatremia is crucial for appropriate diagnosis and treatment. Laboratory tests, including blood sodium levels and a thorough clinical evaluation, help determine the underlying cause and severity of hyponatremia. Treatment focuses on addressing the underlying cause and correcting sodium levels, often through fluid restriction, adjusting medications, or using intravenous saline solutions in severe cases. At 1st case we have found that megestrol acetate causes adrenal insufficiency which in turns causes hyponatremia. Megestrol acetate agent often used in the treatment of certain conditions such as advanced breast cancer, endometrial cancer, and appetite stimulation in patients with cancer-associated anorexia and cachexia. While not a common side effect, there have been reports of megestrol acetate causing hyponatremia (low sodium levels) in some individuals[6]. This occurs due to the medication's potential to influence water and electrolyte balance in the body. Megestrol Acetate is a synthetic progesterone which use for treatment of anorexia in patients with AIDS and malignancy[6]. As it cross reacts with glucocorticoid receptor its increase appetite with a unknown

mechanism[7]. In case of sudden cessation of of MA it can cause AI[8]. Our patient presented with persistent vomiting and she used to take megestrol acetate without any proper indication and she was not on regular follow up of any physician. Hence she developed adrenal insufficiency which caused all her symptoms. There are few reported case of AI with megestrol acetate. A case was reported that a female came with nausea and generalized weakness later diagnosed to have adrenal insufficiency who was taking megestrol acetate hiddenly[10]. They have confirmed it by urinary glucocorticoid screening[10]. The admitting team in this didn't do glucocorticoid screening as the history of the patient and laboratory findings are consistent with the diagnosis.

The 2nd and 3rd we discussed presented with hyponatremia with underlying hypopituitarism. It is not uncommon to have hyponatremia in patients with hypopituitarism. Sometimes it could be the early presentation of the disease who has undiagnosed hypopituitarism[11]. Although it is not known that this hyponatremia is caused by hypersecretion of ADH[12]. The patient (2nd case) presented with repeated history of hyponatremia when he was also diagnosed to have schizophrenia and was under anti psychotic drug. The admitting team initially thought it was a case of SIADH. Later after biochemical investigations it revealed patient had hypopituitarism although the MRI was apparently normal except partially empty sella and other cause was yet to be evaluated due to limitations. According to a reported case, a 69 year old male presented with lethargy and hyponatremia who was initially thought to be having SIADH but even with correction hyponatremia was not corrected and later that patient found to be having hypopituitarism with underlying pituitary macroadenoma[13]. The discussing 3rd case also has underlying pituitary insufficiency who presented with hyponatremia. The admitting team follows the protocol and found to have hormonal deficiencies and treatment started accordingly.

Conclusion:

The cause of hyponatremia is like Pandora Box. The purpose of this case report is to let clinicians know to look for the cause vigorously when the cause is hidden under sea.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study

Funding:

This research received no external funding.

Ethical consideration:

The study was conducted after approval from the ethical review committee of Popular Medical College. The confidentiality and anonymity of the study participant was maintained.

Consent:

For the purpose of publishing this case report and any related photos, the parents are written informed consent was acquired.

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