

Case Report

Unusual paraneoplastic syndrome of inappropriate antidiuretic hormone secretion with gastric cancer

Ananth Pai¹, Saniya Pervin^{2*}

¹Department of Medical Oncology, Kasturba Medical College, Manipal, Karnataka, India

²Department of Medicine, Dr. TMA Pai Hospital, Udupi, Karnataka, India

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*Correspondence:

Saniya Pervin,

E-mail: saniya.safdar1@gmail.com

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ABSTRACT

Syndrome of inappropriate antidiuretic hormone secretion (SIADH) results in impaired water excretion and consequent water intoxication and hyponatremia. In patients with cancer, SIADH is most commonly driven by ectopic ADH production, a paraneoplastic syndrome frequently seen in small cell lung cancer. A 63 year old male presented with loss of appetite, vomiting and hiccups. No abnormalities were detected on physical examination. Upper gastrointestinal endoscopy showed a proliferative growth in the stomach and histopathology report confirmed gastric adenocarcinoma. His laboratory investigations revealed low serum sodium and further work up for SIADH confirmed the diagnosis. The patient was treated with hypertonic saline and he improved symptomatically. He was subsequently treated with two cycles of capecitabine and oxaliplatin. The patient was asymptomatic and maintained a serum sodium in the range of 120 to 130 mEq/L, with a serum sodium of 127 mEq/L on follow up.

Keywords: Antidiuretic hormone, Ectopic secretion, Gastric carcinoma, Hyponatremia, Paraneoplastic syndrome, SIADH,

INTRODUCTION

Syndrome of inappropriate antidiuretic hormone secretion is defined as excessive free water reabsorption in the collecting ducts due to increased antidiuretic hormone secretion relative to serum osmolality.¹ This condition is associated with various malignancies, however, to date, there have been only four case reports in medical literature regarding the association of gastric cancer with SIADH and hence we present this rare clinical scenario.

CASE REPORT

A 63 years old Indian male, hypertensive on treatment with amlodipine presented with complains of loss of

appetite, heart burn, vomiting and hiccups of 1 month duration. His past medical history was non-conductive. On examination, he was hemodynamically stable and had nil localizing abdominal signs. A possibility of peptic ulcer disease versus gastroesophageal malignancy was thought of as differential diagnoses. Investigations done showed anemia (Hemoglobin of 10.6 g/dl) with normal leucocyte and platelet counts. The renal function and liver function tests were normal.

Ultrasonography of the Abdomen showed suspicious hypoechoic lesion in segment II of liver with mild ascites. Upper gastrointestinal endoscopy showed an ulceroproliferative growth involving the antrum and pylorus with extension into the first part of duodenum with the scope being able to passed into D2 part of

duodenum. Histopathology of the growth revealed a well differentiated, papillary type adenocarcinoma. Contrast enhanced CT abdomen showed a heterogeneously enhancing circumferential wall thickening with loss of mural stratification in the antrum, pylorus of the stomach, D1 segment of duodenum causing mild narrowing of the lumen with dilation of proximal stomach and a well-defined hypodense lesion in the segment II of liver with enhancement, suggestive of gastric malignancy with liver metastasis. His biochemical investigations revealed serum sodium of 125 mmol/L with serum creatinine of 1.5mg/dl. He was clinically assessed as euvolemic through physical examination. Serum osmolality was low

at 244 mOsm/kg, urine osmolality was 247 mOsm/kg and urine sodium high at 104 mmol/L. With normal serum cortisol level, normal thyroid function tests and low uric acid level of 1.7mg/dl, the lab results were biochemically consistent with SIADH (Table 1). He was advised to have extra added salt in his diet for the hyponatremia along with fluid restriction. As the sodium levels failed to improve, he was managed with intravenous sodium supplementation with 0.9% normal saline. The serum sodium levels were monitored during correction and the values reached a range of 120-123 mEq/mL after correction as he gradually improved clinically (Table 2).

Table 1: Serum and urine sodium at presentation and subsequent follow-up.

Investigation	Day 1	Day 9	Day 10	Day 13	Day 14	Day 15	Day 16	Day 17	On follow up
Serum sodium, (Normal:136-145mmol/L)	125	119	120	116	111 113	123	122 120	121	127
Serum potassium, (Normal- 3.5-5.1mmol/L)	5.1	4.4	4.3	4.3	4.1 4.2	3.9	4.0 4.0	4.1	4.5
Serum creatinine, (Normal: 0.7-1.2mg/dL)	1.5	0.6		0.6					0.9
Serum urea, (Normal: 16.6-48.5mg/dL)	28	8		10					18

Table 2: Serum and urine biochemistries on follow up.

Investigation	Day 10	Day 13
Serum osmolality (Normal: 270-285mOsm/kg)	244	240
Urine osmolality (Normal: 50-1200mOsm/kg)	247	
Urine sodium random (mmol/L)	104	
Thyroid stimulating hormone (Normal: 0.27-4.2microIU/ml)	1.55	
Serum cortisol random (Normal: 3-23mcg/dL)	16.510	
Uric Acid (Normal: male: 4.4-7.6mg/dL)	1.7	
Lactate dehydrogenase (Normal: 125-220U/L)	312	
Alkaline phosphatase (Normal: 40-130U/L)	196	131
Vitamin B12 (Normal: 197-771pg/ml)	244	
Vitamin D (Normal: 20-50ng/mL)	41.4	

He subsequently received 2 cycles of Capecitabine and Oxaliplatin, which was tolerated well. Post second cycle of chemotherapy, he developed persistent vomiting. An

upper gastrointestinal endoscopy revealed food stasis and severe esophagitis in the distal two thirds of the esophagus. The antrum was narrowed by circumferential thick mucosa and the scope could not be passed beyond the mid antrum. A diagnosis of Gastric Outlet Obstruction was made, and self-expandable metallic stent was placed just proximal to the cephalad end of the tumor. The patient was started on oral feeds and discharged.

DISCUSSION

A diagnosis of hyponatremia is made when serum sodium falls below 135mEq/L, usually caused by the inability to excrete water normally.² Inability to suppress Antidiuretic hormone secretion can lead to hyponatremia when the water intake exceeds the amount that is excreted. The ensuing water retention leads to hyponatremia. The hallmark of SIADH is euvolemic hyponatremia, with low serum sodium and low serum osmolality with inappropriately high urine sodium and high urine osmolality, including low serum uric acid levels. Presence of normal thyroid function and cortisol levels are required for diagnosing SIADH. Review of literature showed that there have been only 4 case reports in literature so far regarding the association of Gastric carcinoma with SIADH. The first case is of a middle aged schizophrenic patient who was diagnosed with gastric carcinoma, initially presenting with hyponatremia

and nephrotic-range proteinuria and the author concluded the patient to have reset osmostat variant of SIADH.¹ In the second patient, the ectopic hormone secretion presented 6 months post exploratory laparotomy which detected peritoneal metastasis.³

In the third case, the gastric carcinoma arose within a tubulovillous adenoma, resection of which resulted in correction of electrolyte abnormality immediately, with the patient maintaining serum sodium in the normal range two years on follow up.⁴ The fourth case was a male with advanced gastric adenocarcinoma associated with the syndrome of inappropriate antidiuretic hormone, showing cancer cells immunostained for the antidiuretic hormone.⁵

The treatment of hyponatremia in SIADH usually comprises of three components, mainly treatment of the underlying disease, if possible, combined with initial therapy to raise the serum sodium. This is followed by prolonged therapy in patients with persistent SIADH after correction of initial hyponatremia. Treatment of underlying causes of SIADH may lead to resolution of hyponatremia. Treatment of infections like meningitis, pneumonia, and tuberculosis may effectively treat the hyponatremia, including cessation of underlying drugs like Selective Serotonin Reuptake Inhibitors. Fluid restriction is the initial step in the treatment of SIADH and a goal intake of 800 ml/day has been suggested.⁶

Intravenous hypertonic saline has been used in case of severe, symptomatic or resistant hyponatremia. The principle followed here is that the electrolyte concentration of the fluid must exceed the electrolyte concentration of urine in addition to that of plasma.⁶ This same principle can be extended to oral salt intake. The effect of hypertonic saline or oral salt tablets can be enhanced if given along with a loop diuretic or a vasopressin receptor antagonist such as Tolvaptan, mozavaptan. The loop diuretics and Vasopressin receptor antagonist impair the renal responsiveness to ADH, lowering the urine osmolality and thereby increasing water excretion.⁶

An Effective therapy of hyponatremia is then followed by a maintenance therapy to prevent possible symptom recurrence. This is done by fluid restriction, oral salt intake, urea, or a loop diuretic therapy. Our patient was managed with isotonic saline infusion along with fluid restriction and he showed subsequent improvement in his clinically condition with the serum sodium levels maintaining around 120- 130 mEq/mL.⁷

CONCLUSION

For an initial presentation, paraneoplastic syndromes are a rare manifestation of gastric cancers. These include dermatologic findings such as sign of Leser- Trelat or acanthosis nigricans, though none of these findings are specific for gastric cancer. Membranous nephropathy,

microangiopathic hemolytic anemia, and Trousseau's syndrome are other paraneoplastic syndromes that has been associated with gastric cancer.⁷ Since SIADH is not commonly seen with gastric cancer, we report this rare association and conclude that in an unexplained SIADH, gastric carcinoma could be an underlying cause.

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