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Sheehan syndrome with Gitelman syndrome, Tackling Additive Morbidity

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Sheehan syndrome (SS) is postpartum hypopituitarism resulting from pituitary gland necrosis caused by severe hypotension due to massive intra or post-partum hemorrhage. Defective NaCl transport in the distal convoluted tubule, due to mutations affecting the thiazide sensitive Na-Cl-cotransporter results in the autosomal recessive salt-losing renal tubulopathy, Gitelman syndrome (GS). These two have been rarely described together. We report the case of a middle-aged woman with both these conditions, resulting in management issues. Physicians encountering unexplained hypokalemia refractory to standard management must consider the possibility of renal tubular disorders.

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Case Report

INTRODUCTION

Sheehan syndrome (SS) is postpartum hypopituitarism resulting from pituitary gland necrosis caused by severe hypotension due to massive intra or post-partum hemorrhage (PPH).[1] It remains common in less developed nations, evolves slowly and is diagnosed late. History of lactational failure and early cessation of menses provide diagnostic clues.[2] The autosomal recessive tubulopathy Gitelman syndrome (GS) is caused by defective distal tubular NaCl transport due to mutated thiazide-sensitive Na-Cl-cotransporter.[3] It is characterized by hypomagnesemia, hypokalemia and hypocalciuria. In contrast to Bartter syndrome (BS), patients with GS are older, have a milder clinical picture, normal or slightly decreased urine concentrating ability, reduced urinary calcium excretion and low serum magnesium.[4] GS requires lifelong salt and potassium supplementation or potassium sparing diuretics. SS and GS present together can pose a management dilemma as well as aggravated morbidity.

CASE REPORT

A previously healthy 35-year-female presented with an episode of hypoglycemia 20 days back, recurrent nausea and vomiting for 15 days, abdominal distention of 10 days duration and decreased responsiveness for 1 day. There was no similar episode in the past or relevant drug-intake history. She had been amenorrhic since her last child birth 10 years back when she also had lactational failure following severe PPH. On examination, she had a poor general condition, tachycardia (112/min), hypotension (70 mmHg systolic), respiratory rate 24/min; was afebrile but dehydrated. Further, axillary and pubic hair were absent. Her GCS was 13 (E4V4M5) but remaining neurological and

systemic examination was unremarkable.

SS was suspected. Her blood glucose (64 mg/dL), normalized with 25% dextrose. Her blood pressure did not respond to either normal saline resuscitation or noradrenaline infusion. Intravenous hydrocortisone was administered as 200 mg bolus followed by 50 mg 6 hourly, after sending serum sample for routine labs and cortisol level (Table). Her blood pressure started improving within 10 minutes, initially maintaining at 92/60 mmHg and reaching 100/64 mmHg after 30 minutes of maintenance fluids.

Arterial blood gas analysis revealed hyponatremia which responded to normal saline. However, while her vitals stabilized, and sensorium improved, hypokalemia persisted for several days in the range of 1.7-2.5 meq/L, despite parenteral and oral supplementation. Meanwhile, magnetic resonance imaging of the brain revealed empty sella. The lab picture at day-6 is shown in **Table.** In the presence of hypokalemic metabolic alkalosis, with elevated urinary chloride with hypophosphatemia, the differentials considered were alkali loading, diuretic therapy, Bartter syndrome and Gitelman syndrome. History did not support the former two. A low 24h urinary calcium (50 mg/d), presence of hypomagnesemia and the patient's age meant GS was more likely. Facilities for genetic testing were unavailable. She was managed with intramuscular magnesium sulphate 1g, 8 hourly for 2 days, oral spironolactone 50 mg (2 times/d), and oral potassium supplementation. Serum potassium which had not responded initially to magnesium supplementation (by day-8), normalized within one day of initiation of spironolactone (day-9) (**Table**). The patient has been doing well on follow-up, with steroid and thyroxine supplementation and oral spironolactone.

DISCUSSION

Sheehan syndrome may present after a variable period of initial insult.[1,5] Gitelman syndrome is relatively rare and characterized by chloride resistant hypochloremic metabolic alkalosis with hypomagnesemia, hypokalemia, and hypocalciuria. Although the general condition of the patient in the current case improved with fluid resuscitation and corticosteroid / thyroxine supplementation, refractory hypokalemia was unmasked. Further work up led to a probable diagnosis of Gitelman

Hematological and Biochemical Parameters in the Patient

Investigation Parameter (Units)	At Admission	Day-6 of Hospital Stay	Day-9 of Hospital Stay
Hb, g/dL	10.1		
TLC, µL	9135 (N64L31)		
Na, mEq/L	111	133.8	136.3
K, mEq/L	2.35	1.84	4.23
Creatinine, mg/dL	1.7	0.7	
Urea, mg/dL	89	18	
FSH, mIU/mL	4.88 (17 - 95)*		
LH, mIU/mL	1.06 (8 - 33)*		
fT3, pg/mL	< 0.1		
fT4, ng/dL	0.3		
TSH, µIU/mL	0.55		
Cortisol, µg/dL	11.0 (4.3 - 22.4)*		
pH		7.51	7.39
pCO_2, mmHg		36.3	38.1
HCO_3, mEq/L		30	22.8
AG, mEq/L		13.3	
Calcium/Phosphate, mg/dL		7.1/1.6	
Mg, mg/dL		1	2.6
Urine Na/K, mEq/L		83/20.8	
24h Urinary Potassium, mEq		25	
Ultrasonography of the Abdomen		No Evidence of CKD	

*Reference range mentioned in brackets.
Abbreviations: FSH, follicle stimulating hormone; LH, luteinizing hormone; AG, anion gap; fT3, free triiodothyronine; fT4, free thyroxine; TSH, thyroid stimulating hormone

syndrome. The first case of the combined disorder reported was a 57-year lady who was successfully treated by hormones and electrolyte replacement. The authors of that particular case suggested a possibility of a genetic link.[6] A combination of inherited tubulopathies with pituitary abnormalities on imaging with normal hormonal profile has been recently described in few case reports.[7,8] Moreover, an association between BS and empty sella has recently been reported in 3 children.[7] While any genetic link between hypopituitarism and Gitelman syndrome is yet to be discovered, the authors would like to emphasize that the coexistence of these two disorders may result in additive morbidity, as in our case. Diagnosis of SS is usually obvious, but GS is often missed because of subtle presentation and only diagnosed during evaluation for incidental biochemical abnormalities. Physicians encountering unexplained refractory hypokalemia must consider the possibility of renal tubular disorders.

CONFLICT OF INTEREST

None.

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None.

PATIENT CONSENT

Written informed consent taken.

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