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Case Report

An acquired Bartter syndrome with secondary Sjögren syndrome

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ABSTRACT

Renal tubular involvement in Sjögren's syndrome (SS) often described with renal tubular acidosis, nephrogenic diabetes insipidus, or rarely with Fanconi syndrome. SS presenting with clinical features of Bartter's syndrome or Gitelman's syndrome is rare. We report a case of a female patient who presented an acquired Bartter syndrome with a secondary SS. Our case highlights the fact that hypokalemia with metabolic alkalosis in an adult patient should prompt clinicians to look for common and uncommon conditions. While assessing for abnormal conditions, acquired Bartter syndrome should be considered if a patient has an underlying autoimmune, endocrine, or connective tissue disease.

Keywords: Bartter syndrome, Sjogren syndrome, Hypokalemia, Hypercalciuria, Metabolic alkalosis

INTRODUCTION

Bartter syndrome is a rare autosomal recessive, salt-losing disorder characterized by hypokalemic hypochloremic metabolic alkalosis. It was first described by Bartter in 1962. The typically associated laboratory abnormalities include marked hypokalemia, metabolic alkalosis, and volume contraction leading to increased serum osmolarity and hyperaldosteronism.[1] Acquired causes of Bartter syndrome include autoimmune disorders like Sjogren syndrome (SS), Hashimoto thyroiditis, scleroderma, and several drugs like aminoglycosides, loop diuretics, and amphotericin.[2,3]

SS belongs to a group of connective tissue diseases. Dryness of mucosa and eyes is the most common and most recognizable symptom of the disease. There are two forms of the disease: primary Sjögren's syndrome (pSS) and secondary Sjögren's syndrome (sSS). Association of barter's syndrome with SS is rare with a prevalence of one in 1,000,000 and very few cases have been reported in literature. We are reporting a case of 25 years old female patient, who presented with multiple joint pain, Bilateral lower limb pitting edema, gritty sensation in eyes, swelling of lips, and ulcerations over tongue and oral mucosa.

CASE REPORT

Informed consent was obtained from the patient and patient's relatives before publishing the case.

The patient, 25-year-old female, resident of Buldhana, Maharashtra, India, homemaker by occupation came to our institution with history of multiple joint pain since 6 months, for which she had visited local clinics and was started on methotrexate, sulfasalazine, leflunomide. She also complained of bilateral lower limbs swelling, pitting in nature, gritty sensation in eyes since 3 months and breathlessness, swelling of lips, and ulcerations over lips, tongue and oral mucosa since 3 days.

Patient was a known case of hypothyroidism since 3 years and was on medication for it.

On examination, her blood pressure was 100/60 mmHg, pulse 76/min, saturation of 82% on room air and she was febrile with a temperature of 101 degree Farenheit. Her body mass index (BMI) was 22 kg/m^2. Chest examination showed no abnormalities except minimal bilateral lower zone crepitations. Rest systemic examination was within normal limits. Her electrocardiography (ECG) was normal.

Ophthalmologist opinion was taken in view of gritty sensation in eyes. Schirmer's test was done which showed dryness in both eyes.

Figure 1: Dried oral mucosa with oral ulcerations.

Table 1 shows low levels of serum potassium, serum sodium and pancytopenia. There is proteinuria, leukocyturia and alkalotic pH on urine R/E. On quantification of proteinuria, urine protein to creatinine ratio showed proteinuria of 3.76 g/g.

Table 1: Detailed investigations of this patient after admission.

Variables	Value
Hemoglobin (g/dl)	**8.4**
TLC (cells/cmm)	**1060**
Platelet count (cells/µl)	**65000**
Serum creatinine (mg/dl)	0.8
BUN (mg/dl)	17
Serum bicarbonate (mEq/l)	19
Serum magnesium(mEq/l)	1.7
Serum sodium (mEq/l)	**139**
Serum potassium (mEq/l)	**2.1**
Serum calcium (mg/dl)	8.1
fT3/fT4/TSh	2.38/1.38/21.09
Serum phosphorous (mg/dl)	3.5
Serum uric acid (mg/dl)	3.3
Blood glucose random (mg/dl)	187
AST (U/l)	57
ALT (U/l)	101
ALP (U/l)	**552**
Total bilirubin (mg/dl)	1.6
Direct bilirubin (mg/dl)	1.0
Indirect bilirubin (mg/dl)	0.6
Urine R/E	Protein: ++, 1-2 WBCs/HPF, **urine PH: 7**, urine specific gravity: 1.010, budding yeast cells seen

Given severe hypokalemia, the patient was given the daily replacement of 80 mEq/l parenteral and 40 mEq/l of oral potassium supplementation. Her serum potassium was also monitored strictly.

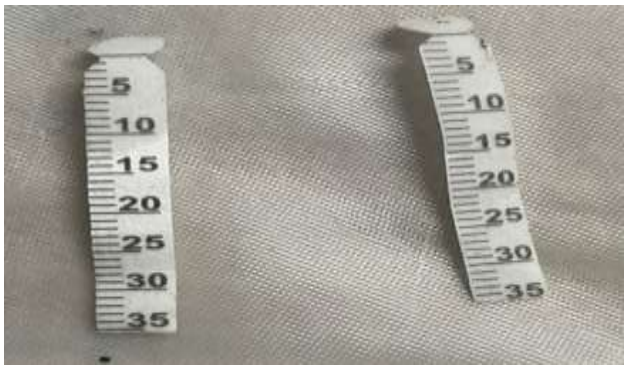

Figure 2: Schirmer's test of both eyes.

For the further workup of her hypokalemia, the following labs were obtained as shown in Table 2.

Table 2: Lab reports.

Variables	Value
Urine sodium(mmol/l)	**145**
Urine potassium(mmol/l)	**43.5**
Urine chloride (mEq/l)	**208 (46-168)**
Serum creatinine (mg/dl)	0.8
BUN (mg/dl)	17
Serum bicarbonate (mEq/l)	19
Urinary calcium (mg/dl)	**26.7**
Urine anion gap	28.9
ABGs	pH: 7.53,
	pO_2:77.6
	pCO_2:32.6
	HCO_3:27.6

Table 3: List of investigations performed on this patient.

Variables	Value
ESR (mm/hour)	**45**
ANA	Negative
CRP	**276.36**
Histones	Negative, 3
ANCA profile	Negative, 2
Ribosome	Negative, 1
dsDNA	Negative, 0
Anti-Smith/RNP antibody	Negative, 1
Anti-PM-Scl antibody	Negative, 2
Anti-RNP antibody	Negative, 2
Anti-dsDNA	Negative
Anti-Ro antibody	Strongly positive, 149
SSA	Strongly positive, 117
SSB	Positive, 32

Table 2 shows high urine sodium, potassium, chloride and calcium. As the urine pH was also alkalotic, a diagnosis of

Bartter syndrome was suspected. A detailed autoimmune workup was performed.

The diagnosis of connective tissue disorder was made based on raised levels of ESR, CRP, positive anti-Smith/RNP antibody, SSA, SSB.

She was started on carboxymethylcellulose eye drops, saline compressions followed by fusidin cream over lips, triamcinolone acetonide mouth paste for buccal mucosa lesions. She was treated with intravenously potassium supplementation, spironolactone and azathioprine. She was normokalemic after 15 days of hospital discharge. Her Lip and oral mucosal lesions improved.

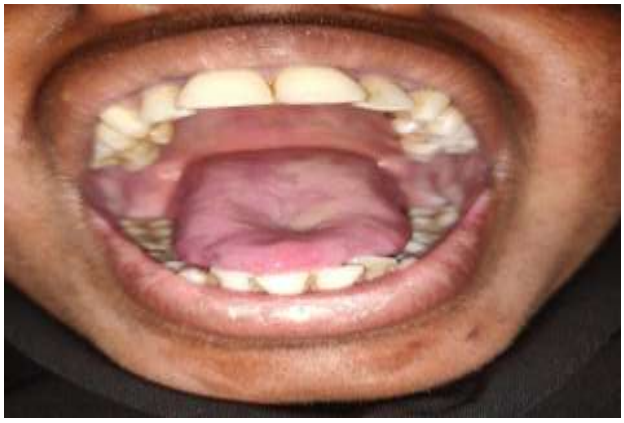

Figure 3: Oral Mucosa on follow up.

DISCUSSION

Bartter syndrome is a rare autosomal recessive disorder with a prevalence of one in 1,000,000 described by Bartter in 1962, resulting from mutations affecting any of the five ion transport proteins in the apical membrane of thick ascending loop of Henle resulting a salt-wasting and hypokalemic metabolic alkalosis.

Based on the different underlying disease-causing genes, Bartter syndrome was classified into five types.[4-8]

Type I results from mutations in the SLC12A1 gene and due to defective function of the Na-K-2Cl cotransporter.

Type II is caused by mutations in the KCNJ1 gene and due to defective function of the renal potassium channel (ROMK).

Type III results from mutations in the CLCNKB gene and due to defective function of the renal chloride channel (CIC-kb).

Type IV is caused by mutations in the BSND gene or from a combination of mutations in the CLCNKA and CLCNKB genes and due to reduced activity of both ClC-Ka and ClC-Kb transporters.

Type V is caused by mutations in the calcium-sensing receptor (CASR) gene and due to defects in the CaSR in the basolateral membrane of the thick ascending limb.

The laboratory criteria of Bartter syndrome can include hypokalemia with hyperkaliuria, hyponatremia, hypochloremia, metabolic alkalosis, mild hypomagnesemia, hypercalciuria, hyperaldosteronism, hyperreninemia with normal blood pressure. Most of these abnormalities (hypokalemia, hyperkaliuria, hyperchloremia, hypercalciuria, metabolic acidosis) were found in our patient.

In contrast to Bartter syndrome, Gitelman syndrome is a disorder affecting the distal tubule and is caused by mutation in the SLC12A3 gene, which encodes the thiazide-sensitive NaCl cotransporter. This disorder is associated with hypokalemic, metabolic alkalosis, hypocalciuria, and hypomagnesemia.[9]

SS is an autoimmune disease which predominantly affects middle-aged women, with a female-to-male ratio reaching 9:1.[10] This disease is characterized by sicca symptoms (dryness of the eyes and mouth) caused by lymphoplasmacytic infiltration of the exocrine glands (salivary and lachrymal) and production of antibodies.[11] All tissues may be affected, including kidneys, gastrointestinal system, blood vessels, lungs, liver, pancreas, and nervous system. The reported prevalence of renal involvement ranges from 2% to 67%.[12] One of the most common reported renal manifestation is interstitial nephritis.[12] Acquired Bartter syndrome associated with SS is rare. Our case highlights the fact that hypokalemia with metabolic alkalosis in an adult patient should prompt clinicians to look for common and uncommon conditions.

CONCLUSION

While assessing for abnormal conditions, acquired Bartter syndrome should be considered if a patient has an underlying autoimmune, endocrine, or connective tissue disease.

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