Case Report

Hypokalemic respiratory paralysis due to distal renal tubular acidosis as the presenting manifestation of Sjögren’s syndrome

Gourav Goyal, Rama Kant, Atulabh Vajpayee*

Advanced Neurocare Institute, GBH American Hospital, Udaipur, Rajasthan, India

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Abstract

Hypokalemic respiratory paralysis in Sjögren’s syndrome (SS) with distal renal tubular acidosis (RTA) is very rare. In the literature, only five such cases have been reported. We report a 48-year-old lady, who presented with respiratory paralysis, bulbar weakness, and flaccid quadriplegia. She had severe hypokalemia (1.11 mEq/L), metabolic acidosis (pH = 7.09), hyperchloremia (120.8 mEq/L), and normal anion gap (11.2). An ammonium chloride test was consistent with the diagnosis of distal RTA. She recovered completely with potassium and alkali supplementations. Clinical features, positive Schirmer’s test, and autoantibody screening were suggestive of diagnosis of SS. Hypokalemic periodic paralysis and respiratory involvement may occur as a first and rare complication of SS with distal RTA. Immunosuppressive therapy is not indicated except in the presence of systemic vasculitis. Potassium and alkali supplementations are the mainstay of the therapy. Patients with secondary hypokalemic periodic paralysis should be investigated for this possibility.

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1. Introduction

Sjögren’s syndrome (SS) is an autoimmune disorder primarily involving exocrine glands. It may have various extraglandular manifestations and renal abnormalities are one of them. Both glomerular and tubular involvement have been reported in SS, although tubular involvement is more common. SS leads to lymphocytic and plasma cells infiltration in renal interstitium. Interstitial nephritis is responsible for occult or overt tubular manifestations in SS. Renal manifestations in SS may vary from distal renal tubular acidosis (RTA), nephrolcacinosis, nephrogenic diabetes insipidus, and uncommonly proximal RTA. Distal RTA results in loss of potassium due to impaired acidification in distal tubules. Hypokalemia may result in flaccid quadriparesis and rarely respiratory paralysis. We report a rare case of Sjögren’s syndrome with distal RTA and hypokalemic respiratory paralysis.

2. Case report

A 48-year-old woman presented in the emergency room with complaint of progressive weakness of all four limbs for 1 day. She first noticed difficulty in getting up from a squatting position, followed by difficulty in walking. Within the next few hours, she developed weakness of both upper limbs. By evening, she became bed bound. In the emergency room, she had difficulty in breathing with an inability to speak a complete sentence. She had history of vomiting (2 or 3 episodes/day) for the past 2 days. She had no prior history of such episodes, hypertension, diabetes mellitus, or any other chronic illness. In the emergency room, blood pressure was 150/86 mmHg, pulse rate 96/minute, respiratory rate 24/minute, and SpO₂ was 98% on 2 L oxygen. She was conscious and...
alert on admission. Cranial nerve examination revealed bulbar weakness. She had muscle power of Medical Research Council Grade 0 in all four limbs proximally as well as distally. Deep tendon reflexes were absent with mute plantars. Sensory examination was normal. Cardiovascular system and abdomen examination did not reveal any abnormality. Within a few hours of hospitalization, her respiratory distress worsened with respiratory rate of 30/minute with shallow excursions and SpO₂ 84% on 8 L oxygen. Because of respiratory involvement, she was intubated and put on mechanical ventilation. Arterial blood gas analysis revealed a pH of 7.09, HCO₃⁻ 9 mmol/L, chloride 120.8 mEq/L, and an anion gap of 11.2. Her initial potassium value was 1.11 mEq/L. Other investigations revealed serum sodium of 141 mEq/L, ionized calcium 5.2 mg/dl, serum magnesium 2.44 mg/dl, inorganic phosphate 4.05 mg/dL, and alkaline phosphatase 116.2 U/L. The total serum proteins were 6.5 g/dL (globulin 3.06 g/dL and albumin 3.44 g/dL). Electrocardiogram showed ventricular ectopic, ST segment depression, wide QRS complexes, and prolonged QTc interval and U waves (Fig. 1). Cardiac markers were negative (creatine phosphokinase-MB = 2.34 ng/mL and troponin T = 0.055 ng/mL). Renal function and liver function tests were normal. The erythrocyte sedimentation rate was 50 mm in the 1st hour (normal = 20 mm). Urinalysis did not show proteinuria. Urine pH was 6.8, random urine sodium 67.4 mEq/L, random urine potassium 32 mEq/L, random urine chloride 89.4 mEq/L, and urine HCO₃⁻ 4.5 mMol/L. Urine anion gap was positive (10). Difference between urine and blood PaCO₂ was 6.9 mmHg. Fractional excretion of bicarbonate (FEHCO₃⁻) and fractional excretion of potassium (FEK⁺) were 1.58% and 96%, respectively. Diagnosis of distal RTA was made in the presence of hyperchloremic metabolic acidosis, normal anion gap, high urine pH (> 5.5), positive urine anion gap, urine and blood PaCO₂ difference < 20 mmHg, less FEHCO₃⁻ (< 5%) and increased FEK⁺.

She was managed with potassium (both intravenous and oral) and alkali supplementations. Her sequential serum electrolytes are recorded in Table 1. Following correction of hypokalemia, her muscle power and respiration improved. She was weaned off the mechanical ventilator after 24 hours. After extubation, her history was again enquired. She had history of dry eyes and mouth for 2 months without associated joint pains, joint swelling, photosensitivity, or recurrent oral or genital ulcerations. Schirmer’s test showed lacrimation of 4 mm in 5 minutes. Ammonium chloride test was performed after normalization of arterial pH. Loading of ammonium chloride (100 mg/kg) resulted in a fall of the arterial pH from 7.41 to 7.34 with a persistently high urine pH > 7.5. The ammonium chloride test was consistent with diagnosis of distal RTA. Autoantibody screening revealed positive antinuclear antibody titer of 4.18 by enzyme-linked immunosorbent assay method (positive > 1.20). Anti-Ro (SS-A) and anti-La (SS-B) antibody were strongly positive with titers of 96.64 U/mL (> 8 = positive) and 99.26 U/mL (> 8 = positive), respectively. Anti-double-stranded DNA antibody and rheumatoid factor were negative. Thyroid function tests were normal (thyroid stimulating hormone = 4.2 μIU/mL). Ultrasonography of the abdomen did not reveal any urinary tract abnormality. No radiopaque shadow of the renal calculus was visualized on plain skiagram of the abdomen. Salivary gland biopsy and sialography were deferred by the patient. Clinical features and high autoantibody titers were consistent with a diagnosis of SS.

![Fig. 1.](image-url) (A) Electrocardiogram of the patient at admission shows changes of severe hypokalemia including presence of U wave, ST segment depression, wide QRS complexes (120 ms), prolonged QTc interval (69 ms), and ventricular ectopic. (B) Normalization of the electrocardiogram changes after correction of the hypokalemia.
The patient was maintained on potassium citrate solution and sodium bicarbonate supplementations. Immunosuppressant therapy was not considered in the absence of other systemic features. At 6-month follow-up, she had no recurrence of hypokalemic periodic paralysis and was independent for daily activities.

3. Discussion

Our patient had flaccid quadriplegia with respiratory involvement secondary to severe hypokalemia due to distal RTA. The diagnosis of distal RTA was suspected on the basis of hyperchloremic metabolic acidosis, normal anion gap, and persistently high urine pH >5.5. Confirmation of the diagnosis of distal RTA was made by ammonium chloride test, which resulted in acidemia with failure of acidification of the urine. Diagnosis of SS was made by the findings of oral and ocular symptoms, positive Schirmer’s test, and high auto antibodies (anti SS-A/SS-B autoantibody) titer.

RTA has been subdivided into distal (type 1), proximal (type 2), and secondary to aldosterone deficiency or resistance (type 4). Among these, distal RTA is the most common form. Distal RTA has two forms, complete or classical and incomplete or latent form. Incomplete distal RTA is not associated with systemic acidosis. Classical distal RTA has multiple underlying etiologies. These include primary or idiopathic forms and more commonly secondary to autoimmune disorders, hyper- or hypocalcemia, paraproteinemia, and drug or toxin exposure. Autoimmune disorders such as Sjögren’s disorder and rheumatoid arthritis are the most common cause of acquired distal RTA in adults. Although distal RTA occurs in 25–40% of patients with SS, it is rarely clinically apparent. Hypokalemia is the presenting manifestation of SS in < 2% of the cases.

Different provocative tests are used to differentiate renal tubular acidosis types. These tests include loading of ammonium chloride, bicarbonate, arginine hydrochloride, calcium chloride, sodium sulfate infusion, and furosemide. In this particular case, we used the ammonium chloride test. In the blood, ammonium chloride dissociates into ammonia and H\(^+\) ion. Accumulation of the H\(^+\) leads to the metabolic acidosis. In the distal RTA (type-1), urine pH remained persistently high despite of systemic metabolic acidosis because of the defect in distal tubular acidification.

The first case of hypokalemic periodic paralysis as initial manifestation of the SS was reported in 1981. With time, more cases of hypokalemic periodic paralysis secondary to the SS were reported. In one case series of 31 patients of hypokalemic periodic paralysis from India, three cases had SS. In another retrospective series of 52 patients of hypokalemic periodic paralysis from India, seven (13.5%) had distal RTA (type-1). Secondary hypokalemic periodic paralysis had more severe hypokalemia compared to the idiopathic form. To the best of our knowledge, so far only five cases of hypokalemic respiratory paralysis due to SS have been reported. Our case is the sixth. All the reported cases including the present case were females aged 27–56 years. Minimum serum potassium level was < 2 mEq/L in all cases except one (Table 2).

Potassium and alkali supplementations are indicated in all the cases of SS and RTA. Immunosuppressive therapy is not indicated in this particular situation except in the presence of systemic vasculitis. In the literature, there are reports of immunosuppressive therapy for RTA with SS without a change in outcome. In one report, two out of the 10 patients with interstitial nephritis were treated with intravenous cyclophosphamide. There was little change in renal abnormalities. In another case report, a patient with hypokalemic respiratory paralysis secondary to SS was treated with steroids for 6 months but the patient had recurrence of symptoms after stopping potassium and alkali supplementations. Our patient recovered with potassium and alkali supplementations. In the absence of features of systemic vasculitis, immunosuppressive therapy was not considered.

In conclusion, hypokalemic respiratory paralysis in SS is very rare. We report this rare case to highlight the fact that SS can present the first time as respiratory paralysis secondary to distal RTA induced hypokalemia. Every case of hypokalemia secondary to distal RTA should be evaluated clinically and investigated for SS particularly in the case of severe hypokalemia.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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References