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HYPOKALEMIC PARALYSIS AS A PRESENTING FEATURE OF PRIMARY SJOGREN'S SYNDROME: A SERIES OF 6 CASES

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ABSTRACT We describe here a series of 13 cases who presented with hypokalemic paralysis secondary to distal Renal tubular acidosis(RTA). All the patients presented with quadriparesis and were found to have hypokalemia on investigation. Blood gas analysis revealed the picture of acidosis with normal anion gap and urinary pH > 5.5, suggestive of distal RTA. All the patients received intravenous potassium and bicarbonate supplementation and quadriparesis improved over 4-72 hours. Out of the 13 cases, etiology of distal RTA was found to be Primary Sjogren's syndrome(PSS) in 6 cases. All the 6 patients were positive for anti-Ro or anti-La antibodies, and lip biopsy was positive in 3 patients. History of sicca symptoms was present only in 2 of the 6 patients. In our series Sjogren's syndrome accounted for 46.1% of RTA cases. Renal involvement in Sjogren's syndrome is common and may precede sicca symptoms. Sjogren's syndrome is one of the best documented cause of distal RTA.

To conclude, renal involvement in PSS can uncommonly present as hypokalemic paralysis in the absence of significant sicca symptoms or may precede sicca symptoms.

KEYWORDS : Hypokalemic paralysis, distal RTA, Primary Sjogren's syndrome

INTRODUCTION:

Sjogren's syndrome is a chronic, slowly progressive autoimmune disease characterized by lymphocytic infiltration of the exocrine glands resulting in xerostomia(dry mouth) and dry eyes. The majority of patients with Sjogren's syndrome have symptoms related to diminished lacrimal and salivary gland function(1). Middle-aged women (female-to-male ratio, 9:1) are primarily affected, although Sjogren's syndrome may occur at any age, including childhood(1). Primary Sjogren's syndrome (pSS) is distinguished from secondary Sjogren's syndrome (sSS) which occurs as a part of other autoimmune diseases. sSS coexists especially with systemic lupus erythematosus (15–36%), rheumatoid arthritis (20–32%) as well as limited and progressive systemic sclerosis (11–24%), less frequently with multiple sclerosis and autoimmune hepatitis and thyroiditis(2). Extraglandular manifestations are seen in one-third of patients with Sjogren's syndrome. The most common extraglandular manifestations are arthralgia and polyarthritis, pulmonary involvement , cutaneous vasculitis, renal involvement and neurological(sensory neuropathy) (3). Renal involvement varies widely between 5% to 50% of patients with Sjogren's syndrome[4- 6]. Renal manifestations in Primary Sjogren's syndrome can be heterogeneous, varying from mild electrolyte abnormalities to complete distal renal tubular acidosis (d RTA), interstitial nephritis (IN) or glomerulonephritis (GN) [4]. Sjogren's syndrome is one of the best-documented acquired causes of classic d RTA. Our present case series describes a series of 13 cases presented with hypokalemic paralysis and distal RTA and Primary Sjogren's syndrome was diagnosed to be the cause in 6 cases.

CASE SERIES:

We describe here a series of 13 cases who presented with hypokalemic paralysis secondary to distal RTA. All the patients presented with quadriparesis and were found to have hypokalemia on investigation. The patients were further evaluated with Blood gas analysis, Urinary pH . A diagnosis of distal RTA was made in view of an alkaline urinary pH (>5.5) in the setting of normal anion gap metabolic acidosis. All the patients improved within 24-72 hrs after receiving intravenous and oral potassium supplementation. The etiology of distal RTA was investigated on the lines of Sjogren's syndrome, hypothyroidism, thryrotoxicosis and Systemic lupus erythematosus. Patients were evaluated with Thyroid profile, Serum antithyroid peroxidase antibodies, antithyroglobulin antibodies, anti-Ro/La antibodies, and other antinuclear antibodies quantitative estimation were done after the diagnosis of RTA was confirmed. Patients with positive anti-Ro/La antibodies were advised lip biopsy for minor salivary gland inflammation and Schirmer's test. Schirmer's test <5 mm at the end of 5 min was taken as positive.

Out of the 13 cases of distal RTA, etiology was found to be Sjogren's in 6 cases, Thyrotoxicosis in 1 case, and Idiopathic in 6 cases(after adequate investigation). Primary Sjogren's syndrome(pSS) was diagnosed in 6 patients using the diagnostic criteria laid by the Sjogren's International Collaborative Clinical Alliance (2012)(7).

Out of the 6 cases of Sjogren's, 5 patients were female and one male with a mean age at presentation being 39.3 years (range 26–57).Only two patients(33.3%) had sicca symptoms at the time of presentation. 66.6% (4/6) of patients had no signs and symptoms of exocrine gland involvement and were diagnosed to be Sjogren's syndrome after serology testing. All patients were tested positive for anti-Ro or anti La antibodies, and other antinuclear antibodies were negative. Clinical and laboratory characteristics of these patients were listed in Table 1.

Table 1: Clinical & laboratory data of the 6 patients with Sjogrens and distal RTA

S.no	Age/sex	Antibody PROFILE	Sicca symptoms	Lip biopsy	ABG analysis	Serum Potassium (at presentation)
1.	38/F	Anti Ro +ve Anti La +ve	Absent	Not done	Ph-7.28 Hco3-14.2 Anion gap-11	K - 2.5
2	47/F	Anti Ro +ve	Present	positive	Ph-7.2 Hco3-14.2 Anion gap- 8	K - 1.8

3	26/M	Anti Ro +ve	Absent	positive	Ph-7.3 Hco3-12.9 Anion gap-11	K - 2
4	28/F	Anti Ro +ve	Absent	Not done	Ph-7.37 Hco3-24 Anion gap-8	K - 1.9
5	57/F	Anti Ro +ve	Absent	positive	Ph -7.29 Hco3-13.4 Anion gap- 10.6	K - 2.6
6	40/F	Anti Ro+ve, Anti La +ve	Present	Not done	Ph- 7.1 Hco3- 11 Anion gap- 12	K – 2.2

Histopathology of lip biopsy showed minor salivary gland inflammation with lymphocytic infiltration in 3 patients(Figure 1). Schirmer's test was positive (<5 mm) in one patient. Our results showed Sjogren's as an etiology of distal RTA in 46.1% of patients (6 of 13).

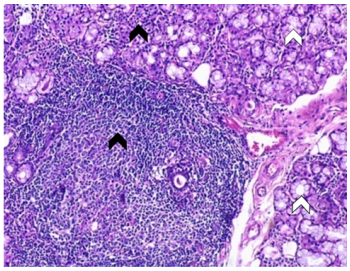

Figure 1: Labial salivary gland biopsy consistent with Sjogren's syndrome, showing multiple lymphocytic foci (black arrow) and intact acinar units (white arrow)

DISCUSSION

A diagnosis of Primary Sjogren's syndrome is often considered based on the classic symptoms of mouth and eye dryness, fatigue, and pain . However, systemic complications sometimes provide the first clue to the disease as seen in our case series, in which the presenting complaint was quadriparesis secondary to severe hypokalemia and metabolic acidosis.

In our series of 13 cases with hypokalemic paralysis with distal RTA, 6 cases were diagnosed to have Primary Sjogren's syndrome. Out of the 6 cases of Sjogren's, five patients were female and one male with a mean age at presentation being 39.3 years. In a study by Jain et al.(5), patients with Sjogren's syndrome and distal RTA(34.9 years) were younger by almost 7 years when compared to Sjogren's syndrome without distal RTA at disease onset and presentation. Similar observation of younger age at presentation in patients of Sjogren's with distal RTA was made in our study. In our series of 6 cases of Sjogren's, only 2 patients presented with sicca symptoms and renal involvement may precede sicca symptoms as shown in other case series in literature(5,8). Renal involvement may be the first manifestation of Sjogren's syndrome.

All cases of distal RTA should be investigated for Sjogren's syndrome as d RTA occurs frequently in patients with Sjogren's syndrome. Distal RTA in patients with Sjogren's syndrome is a result of an immunologic attack on the collecting tubule, causing failure of the H+-ATPase to be inserted into the apical membrane of type A intercalated cells(1).

Distal RTA was seen in 33% and 70% of the cases of Sjogren's syndrome in the series by Maripuri et al. and Ren et al. respectively(9,10).In our series Sjogren's syndrome accounted for 46.1% of RTA cases. In a series by Ram et al., Sjogren's was found to be the etiology of 34.8% of RTA(11). The etiology of distal RTA could be Primary or secondary. Primary distal RTA is seen in children sporadically or with autosomal dominant or recessive transmission (12). Secondary distal RTA occurs in the context of few genetic diseases and in adults, distal RTA frequently develops as a consequence of autoimmune disorders with renal involvement such as Sjogren's syndrome and systemic lupus erythematosus. Hypergammaglobulinemia, Chronic liver disease, particularly chronic active hepatitis and primary biliary cirrhosis, and chronic renal allograft rejection have also been found to be associated with distal RTA(13).

In all our patients, immediate treatment was started after a diagnosis of Hypokalemic paralysis with RTA was made. All the patients were started on intravenous administration of potassium and bicarbonate. Monitoring in ICU was done for 24-48 hrs with ongoing potassium and bicarbonate replacement with regular monitoring of Serum investigations. All the patients improved in limb power over 24- 72 hrs. All the patients were discharged by 10 days and were advised to continue oral Potassium and bicarbonate replacement.

Management of Primary Sjogren's Syndrome is symptomatic. In the acute setting, when the patient presents with hypokalemia, the priority will be to reverse the severe hypokalemia with intravenous potassium supplementation, followed by correction of the underlying acidosis. Long-term use of potassium supplementation might be required and combination of corticosteroids and other immunosuppressive drugs has been reported to slow the progression of renal damage in Sjogren's syndrome(10).Agents that are commonly used include hydroxychloroquine, prednisolone, methotrexate, mycophenolate sodium, azathioprine, and cyclosporine.

All the 6 patients with Sjogren's syndrome in our series had normal renal function at presentation and were started on prednisolone 0.5 mg/kg/day and on maintenance doses of sodium bicarbonate and potassium citrate and were on follow up.

This study had a few limitations like small sample size and being a single institutional study. Renal biopsy was not done in the patients and long term impact of renal involvement needs follow up and evaluation.

CONCLUSION:

Primary Sjogren's syndrome patients with distal RTA appear to be a distinct subgroup presenting at an early age with renal manifestations, less of sicca and articular manifestations. Renal involvement in PSS can uncommonly present as hypokalemic paralysis in the absence of significant sicca symptoms or may precede sicca symptoms. Sjogren's syndrome should be investigated in any patient presenting with hypokalemic paralysis from distal RTA, even in the absence of the sicca syndrome.

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