PRIMARY SJOGREN'S SYNDROME AND DISTAL RENAL TUBULAR ACIDOSIS: PRESENTING WITH NEPHROGENIC DIABETES INSIPIDUS SECONDARY TO SEVERE HYPOKALEMIA-A CASE REPORT.

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INTRODUCTION: Sjogren's syndrome is a slowly progressing autoimmune disease characterized by lymphocytic infiltration of the exocrine glands, mainly the lacrimal and salivary glands, resulting in their impaired secretory function. Simultaneously, systemic involvement and symptoms of cutaneous, respiratory, renal, hepatic, neurologic, and vascular systems often occur.[1] This syndrome can present either alone (as primary Sjogren's syndrome) or in the context of an underlying connective tissue disease (as secondary Sjogren's syndrome).[2] Renal involvement is a well recognized extra glandular manifestation of primary Sjogren's syndrome (pSS). Most common manifestations are related to tubular dysfunction, resulting from chronic interstitial nephritis, which can manifest as distal renal tubular acidosis (dRTA), proximal RTA(pRTA), tubular proteinuria, or nephrogenic diabetes insipidus.[3,4] Hypokalemic periodic paralysis, urolithiasis, or osteomalacia are uncommon renal manifestations of pSS.[1] Here, we present a case of primary Sjogren's syndrome predominantly presenting as a renal manifestation in the form of nephrogenic Diabetes Insipidus secondary to severe hypokalemia due to dRTA.

CASE REPORT: A 35-year-old female from poor socio-economic family, mother of 4 children presented with increase frequency of micturation with excessive thirst and intermittent dysuria since 7 years. On several occasions, she was investigated with blood sugar estimations, was normoglycemic every time. She also gave history of progressive generalized and proximal muscle weakness of upper and lower limbs for the past 4 years and increasing difficulty during walking for the past 3 years. There was history of significant loss of weight and became emaciated with marked atrophy of muscles in all extremities (proximal > distal), backache and bone pain, loss of appetite which she attributed to excessive water intake. With the progressive nature of the disease, she became bed-ridden for last 6 months. She also complained of dryness of mouth and gritty sensation of eyes for past 6 months. She was amenorrheic since 4 months. There was no history of fever, joint pain, skin rash, photosensitivity, or parotid swelling. Power in all the muscle groups was markedly reduced but the sensory examination was normal.

DISCUSSION: In view of history and investigations, possibility of renal tubular dysfunction secondary to distal RTA was considered. Diabetes Mellitus was again first ruled out. Routine investigations revealed severe hypokalemia with "U" wave in ECG with normal Na^+ level. Subsequent ABG showed severe non anion gap metabolic acidosis with severe hypokalemia. Her urine PH was 6.5(not fully acidified to the extent of severe systemic acidosis) while plasma PH was 7.0. She also had severe kaliuresis (24 hrs urinary K^+ of 468mEq/24 hrs (normal→25-125) in the setting of severe hypokalemia (K^+=1.4meq/L). Thus, renal tubular dysfunction secondary to dRTA was confirmed. Proximal RTA was not considered as her urine was negative for any reducing substance and protein. To find the cause for dRTA, immunological markers were checked, ANA, Rheumatoid factor were positive, however anti-ds DNA was negative, ESR was elevated, indicating an immunological origin. Since the association between dRTA and pSS is well documented, specific markers for Sjögren's syndrome i.e. Anti SS-A/Ro and Anti SS-B/La were further checked. The result was strong positivity for Anti SS-B/La (2.8). Mucosal biopsy from lower lip for lymphocytic infiltration of the minor salivary glands showed chronic sialadenitis with evidence of epimyoepithelial islands and fibrosis strongly suggestive of Sjogren's disease. Dry eye was confirmed by Schirmer's test which was strongly positive (1mm at 5mins).As the literature suggests the association of dRTA (also Primary Sjogren's) with MBD[8-14], skeletal survey was also performed which showed moderate anterior wedging of the vertebral bodies(Lund 's criteria) and USG picture of bilateral renal microliths. DEXA Scan was not performed as this facility was not available at that time. However, the overall findings suggest the co-existence of MBD with dRTA. So, our patient presents with nephrogenic diabetes insipidus resulting from severe hypokalemia associated with dRTA secondary to primary Sjögren's syndrome with co-existing MBD. Initially, K^+ supplementation was done parenterally followed by Shohl's solution; the dose was titrated according to the clinical and biochemical parameters. Significant improvement in the general condition was achieved within three weeks, able to walk unassisted in one month's time. Osmotic symptoms completely subsided in 6 weeks. She is on regular follow up with Shohl's solution and calcium and Vitamin D supplementation.

ANSWERS TO THE QUIRIES ASKED:

1. Severe hypokalemia was considered as the cause for myopathy in my patient as the patient's proximal muscle weakness improved completely on correction of the hypokalemia. CPK, EMG and NCV were not performed as the weakness improved considerably.
2. SS-B (Anti-La) Ab was strongly positive (2.8) and SS-A (Anti-Ro) was negative (0.4). It was a mistake in the printing (apologise for the same). Corrected version is sent for review again. Primary Sjogren's mentioned in my article still holds true.
3. Rheumatoid factor positivity in primary Sjogren's is also known even though it may suggest secondary to Rh arthritis. Further my patient did not have any history of joint pain and early morning stiffness. Anti-CCP was performed and was negative.
4. ANA can again be positive as a part of an autoimmune connective tissue disease. My patient did not have any features suggestive of SLE.

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Table 1:- Physical parameters	
Weight	28kgs
Height	151cm
BMI	12.28k/m^2
Pulse	74/min
BP	100/60mmHg
Thyroid	Normal size
Parotids	Not enlarged
Teeth	normal
Muscles	Generalized atrophy
Power	2/5
Deep tendon Reflexes	absent

Table 2:- Laboratory parameters			
Hb	12.6gm%	Na^+	140
TLC	9830	K^+	1.4
Plt	3.11lacs	Cl^-	109
ESR	45	Bil	1.0
FBS	95	SGOT	27
HbA1c	5.6%	SGPT	33
FT4	11	GGT	28
TSH	0.6uIU/ml	ALP	66
S.Urea	20	T. Prot	7.4
S.Creatinine	0.7	Alb	3.9
ECG	"U" wave	Cal	8.6
$25(OH)_2D_3$	26 ng/dl	Schirmer's test	1mm at 5mins
Urine RE	Glucose-nil		
	Protein-nil		
	Sp gr-1005		
	PH-6.5		
CXR P/A	NAD	24hrs urinary K^+	468mEq/24 hrs(25-125)
USG W/A	Bil renal microliths, cholelithiasis	24hrs urinary Na^+	1872mEq/24hrs(40-220)
X-Ray D/L spine	Ant. wedging of the vertebrae	24hrs urinary creat	275mg/kg/24hrs(11-20)
RA factor	+ve	Plasma osmolality	281.3mosm/kg(270-300)
CRP	-ve	Urine osmolality	126 mosm/kgH_2O
ANA	-ve	Anti SS-A/Ro	0.4(Negative)
Anti ds DNA	+ve	Anti SS-B/La	2.8 (Strongly positive)

Table 3:- Serial serum Na^+ and K^+						
serum Na^+	140	140	136	140	135	136
serum K^+	1.4	2.2	2.4	2.8	3.0	3.6

Table 4:- Serial ABG				
PH	7.0	7.2	7.34	7.4
HCO3	15.8	15.9	17.2	18.6
pCO2	32.6	33.9	29	30
pO2	81	78	84	92
Na+	140	134	135	136
K+	<2	2.8	3.0	3.6
Cl^-	109	105	103	104
iCal	0.92	0.8	1.0	1.2