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Hypokalemic Periodic Paralysis and Osteomalacia with Osteoporosis in Distal RTA as Initial Presentation of Primary Sjögren's Syndrome: A Case Report

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Abstract

Background: Sjogren's syndrome is a systemic autoimmune disorder of the exocrine glands with extra glandula rinvolvement in one fourth patients. Tubulointerstitial nephritis being the most common Renal pathology. The purpose of the study to reminding readers of this issue and emphasize the necessity for further research on how to deal within the best way.

Case Presentation: A-30 years-aged female patient presented with recurrent hypokalemic paralysis with persistent symptoms due to coexisting osteomalacia. Distal Renal Tubular Acidosis type 1 (dRTA1) manifests as an extraglandular presentation of Sjögren Syndrome (SS). The case focused that in the setting of recurrent hypokalemia, progressive weakness should differentiate from primary hypokalemic paralysis and evaluated for dRTA1, as this conditions are potentially treatable.

Conclusion: Recurrent hypokalaemic paralysis is a rare presentation of primary Sjogren syndrome and it poses a challenge to diagnosisdue to existing diagnostic criteria.

Key words: Distal RTA; Primary Sjogren syndrome; Recurrent hypokalaemia.

Introduction

Sjögren Syndrome (SS) is characterised by grittiness of the eyes and dryness of the mouth due to lymphocytic infiltration of lacrimal andsalivary glands, that leads to glandular fibrosis and exocrine failure. There is systemic features ofneurologic, respiratory, cutaneous, renal, hepatic and vascular event often occur. This syndrome can manifest either as primary Sjögren's syndrome or in the form of underlying connective tissue disease (Secondary Sjögren's Syndrome). Renal involvement is the most common extra glandular manifestation of primary Sjögren's Syndrome, mostly resulting from chronic interstitial nephritis and can present as distal Renal Tubular Acidosis (RTA) tubular proteinuria, proximal RTA. Recurrent hypokalemic paralysis and osteoporosis rarely present as the initial manifestation of a renal tubule pathology due to pSS. Here we present our case, who admitted to CMCH for evaluation of recurrent Hypokalemic paralysis and on further work up found to have distal RTA, with osteoporosis and osteomalacia secondary to pSS on additional work up.

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Case Presentation

A 30 years aged female patient was admitted to Chittagong Medical College Hospital in Medicine Department form 23.11.2023 to 30.12.2023 with the complaints of weakness of both lower limbs for 10years and high grade fever, with undue fatigue, dizziness and painless oral ulcer for 5 days. There was no history of cough, dysuria, bleeding manifestation, joint pain, photo sensitivity, skin rash or parotid swelling. Patient was taking Azathioprine for last one month before presenting to hospital. At presentation to hospital highest recorded temperature was 102°F and was severely anemic with oral ulcer involving oral mucosa and hard palate, her pulse was 110 beats/min, Blood pressure 90/60mmHg, respiratory rate 18 breaths/min. Systemic examinations involving cardiovascular system, Respiratory system, abdominal examination was normal. On neurological examination muscle bulk and tone of all four limbs were normal, muscle power is 4/5 in both upper and lower limbs. Deep tendon reflexes normal in upper limbs, diminished in both lower limbs, Planter is bilateral flexor. Musculoskeletal system examination there was unspecified abnormal gait likely to be waddling gait.

Her lab reports showed Hb -6.5g/dl, WBC-2240/cumm, Neutrophil 8%, Lymphocytes 88%, Platelets 10000/L, Urine PH-7.5, pus cell: 5-6/HPF, RBC: 5-6/HPF, S. Electrolytes (Na+-136 mmol/L, K+-2.32 mmol/l, Cl-102 mmol/l, HCO3-21 mmo/l)

She was treated as drug-induced pancytopenia with neutropenic septic shock. Four units of blood was transfused with injectable Antibiotics, Antiviral, Anti-fungal was given and Azathioprine was stopped. Fever, oral ulcer was cured after five days of supportive treatment but her lower limbs weakness persisted.

The patient was hospitalized 10 years earlier with weakness of both lower limbs and was diagnosed as hypokalemic periodic paralysis. She had Hypokalemia (Documented serum K+ 2.79, 2.2, 4.9, 2.5, 3.15, 2, 2.3 mmol/L, Normal range: 3.5 to 5.5 mmol/L). First attack was acute in onset, with weakness of all four limbs and required support in doing her daily activities. Her menstrual cycle was normal. Her family history was unremarkable. There was no history of recurrent oral ulcer, eye problem. On examination there was no uveitis, oral ulcers, lacrimal or parotid gland enlargement.

For last 3years, weakness increased in both duration and frequency and was progressive and involve mostly both lower limbs. There was no bowel, bladder or sensory involvement during these episodes.She was initially treated with potassium supplements without significant improvement. After further evaluation patient was treated as a case of chronic inflammatory demyelinating polyneuropathy with Glucocorticoid pulse therapy and Azathioprine. But her CSF study and Nerve conduction study was normal.

Further workup (Tables below) showed Hyperchloraemic normal anion gap metabolic acidosis and hypokalemia, Urinary PH >5.5 on several occasions.

ANA Hep2 -strongly positive, coarse speckled pattern. After that patient was referred to specialized center where patient recommended to do ENA profile. Anti-SSA and Anti-SSB became positive. DEXA showed low bone mass in both femoral neck (Z score -2.0 in right femoral neck, Z score -2.2 in left femoral neck)

● Laboratory Parameter of Patients

No	LAB PARAMETER	Result	Normal Value
1.	CBC	Hb: 11.4 g/dL	Female: 11.5 – 15.5 g/dL
		WBC: 9 X 10^9/L	4 – 11 X 10^9/L
		Platelet: 170 X 10^9/L	150 – 450 X 10^9/L
2.	Urine R/M/E	PH: 6	
		Pus Cell: 1 – 2	
		RBC: Nil	
3.	Serum Creatinine	0.99 mg/dL	Female: 0.57 – 1.11 mg/dL
4.	Serum Electrolytes	Sodium (Na^+): 137	136 – 145 mmol/L
		Potassium (K^+): 2.6	3.5 – 5.5 mmol/L
		Chloride (CL^-): 112	98 – 107 mmol/L
		Bicarbonate (HCO_3^-): 18	22 – 28 mmol/L
5.	Electrolytes Spot Urine	Sodium (Na^+): 137	40 – 220 mmol/24h
		Potassium (K^+): 34	25 – 125 mmol/24h
		Chloride (CL^-): 93	110 – 250 mmol/24h
6.	Rheumatoid Factor (RF)	11.87 IU/ml	< 30 IU/ml
7.	CPK	17 U/L	Female: 29 – 168 U/L
8.	Anti SSA Antibody	> 200 u/ml	> 25 u/ml: Positive
9.	Anti SSB Antibody	26.6 u/ml	> 25 u/ml: Positive
10.	Anti SCL 70	2.2 u/ml	> 25 u/ml: Positive
11.	Anti SM	0.4 u/ml	> 25 u/ml: Positive
12.	Anti RNP	1.5 u/ml	> 25 u/ml: Positive
13.	S. Calcium	2.24 mmol/L	2.10 – 2.55 mmol/L
14.	S. Albumin	45 g/l	35 – 52 g/l
15.	S. ALP	70 U/L	Female > 15Y: 40 – 150 U/L
16.	PHT	58.7 pg/ml	15 – 68.3 pg/ml
17.	Vit. D	33.5 ng/ml	Deficiency: < 10ng/ml
			Insufficiency: 10 – 29
			Sufficient: 30 – 100
			Toxicity > 100
18.	S. Magnesium	0.73 mmol/L	Adult: 0.66 – 1.07 mmol/L
19.	S. Phosphorus	1.6 mg/dL	2.3 – 4.7 mg/dL
20.	HB_S Ag	Negative	
21.	Anti HCV	Negative	
22.	Anti HIV	Negative	
23.	BMD result	Lumbar 1st to 4th vertebrae (AP)	0.940 gm/cm^2 eqi of -1.0 Z score
		Right femoral neck	0.691 gm/cm^2 eqi of -2.0 Z score
		Left femoral neck	0.669 gm/cm^2 eqi of -2.2 Z score
24.	Xray pelvis	Multiple looser's zones	
25.	Nerve conduction study	Normal	
26.	Schirmer test	Positive(<5mm)	
27.	Urine Creatinine	06.12.23 40.24 mg/dl	Ref value: 30-125mg/dL
28.	Urine K+	06-12-23	
		39.9 mmol/L	Ref value: 12-62mmol/L

No	LAB PARAMETER	Result	Normal Value	
29.	24 Hrs Urine Electrolyte		26.11-23	Reference value
		Na+ 130 mmol/24hs	》40-220 mmol/24hs	
		K+ 17.4 mmol/24hrs	》25-100 mmol/24hr.	
		Cl- 116 mmol/24 hrs	》110-250 mmol/24	
30.	SGPT	10.12.2016	01.09.2013	
		38.8 u/L	23 U/L	
31.	S.Electrolyte	04.12.2023	27/11/2023	17.12.2016
	Reference:	Na+ 137	Na+ 137	Na+ 144.8
	Na+ 135-145	K+ 3.9	K+ 2.5	K+ 3.15
	K+ 3.5-5	Cl- 99	Cl 100	C1- 115.5
	Cl- 96-106	HCO3 22	HCO3 24	HCO3 24.5
	HCo3 22-28			
		09.06.2014	01.09.2013	
		Na+ 145.20	Na+ 148	
		K+ 4.90	k+ 2.2	
		Cl 110.10	Cl 114	
		HCo3 26.20	HCO3 26.02	
32.	S. TSH	06 12 2023	10-12-2016	
Reference value:		1.59 uIU/ml	0.750 uIU/ml	
0.35-5.5 uIU/mL				
33.	FT3	06 12 2023	Reference value	
		3.45 pg/ml	Adult: 2.30-4.20 Pg/mL	
34.	F T4	06.12.2023	[Ref. value Adult:	
		1.16 ng/dL	0.78-2.19]	
35.	S. Calcium	04.12.2023	29.11.23	11.08.2016
		8.43 mg/dL	7.6 mg/dl	6.31 mg/dL
		[Adult: 8.80-10-60]		
36.	S. Magnesium	04.12.2023	11-08-2016	
		1.58 mg/dL	1.21 mg/dL	
		[Ref-value: 1.60-2.30]		
HBs Ag		10.12.2016		
		Negative		
37.	S CPK	06.12.2023	15-03-0023	10-12-2016
		12 U/L	37 U/L	95 U/L
		[Ref Male: 35-232		(Normal Range <190 U/L)
		Female: 21-215]		
38.	ANA Hep 2	23-11-23	23.11-13	
		Anti-nuclear antibody	Strongly Positive	
		Strongly Positive.		
		Coarse Speckled		
39.	Anti-ds DNA	30-11-2023	Reference	
		18.6 u/ml	<25 u/ml (Negative)	
			>25 u/ml (Positive)	
40.	RA factor	27.03.2018	14.03.2013	
		Negative	Negative	
41.	CSF Study	16.03.2023		
		Color: Colorless, WBC:02/Cumm, Polymorphonuclear cells:Nil,		
		Mononuclear cells: 100%		
		Protein: 62.6 mg/dl, Glucose: 59 mg/dl. [Ref: 15-45 mg/dl]		

No	LAB PARAMETER	Result	Normal Value	
42.	Urine R/M/E	28-11-23	14.03.23	16.12.2016
		PH-7.0	PH-6.5	Reaction: Acidic
		Pus cell ;0-2/HPF	leukocyte (+)	Albumin: Trace
		Epithelial cell 0-2/ HPF	Pus cell: 4.6/HPF	Pus cell: 6-10/ HPF
		RBC-Nill	Epithelial cell:	Epithelial cell:
			2-5/HPF	4-6/HPF RBC: Nil

43. USB of the whole Abdomen.
(05.12.2023)
Bilateral Mild ecshogenic kidney
kidney size (Right:11.2×4.5cm) (left:11.5× 4.3cm)

44. Nerve Conduction velocity Report: (01.01.2024)- Normal study

45. ABG:Hyperchloremic normal anion gap metabolic acidosis and hypokalaemias

46. ECG:Normal

Patient was started on oral Alendronate and Calcium carbonate with Vitamine D 2000IU twice daily. Potassium citrate was added in her regimen to correct renal tubular acidosis.Our diagnosis in this case is possible or incomplete Sjogren's syndrome (As she lacks few clinical features on examination) causing type-1 RTA (Distal RTA) with recurrent hypokalemia with osteopenia.

During follow up her potassium level got normalized to 4.11 mmol, Bicarbonate improved to 25.3 mmol/l. We will get her repeat DEXA scan next month to see any improvement in her bone mineral density.

Discussion

Primary Sjögren's Syndrome (pSS) is an autoimmune disease with protean clinical manifestations.[1] The estimated prevalence of pSS ranges between 0.5 and 2% in various populations, however it remains undiagnosed in a large majority of patients.[2] Two-third of patients with pSS develop extraglandular manifestations.[1] Overt renal involvement in pSS is uncommon and recent literature estimated a clinically significant involvement in 5% of cases.[3] Tubular and less commonly, glomerular disease have been reported. Interstitial nephritis is the most commonly reported histopathological abnormality.[3,4] Other manifestations such as Renal Tubular Acidosis (RTA) nephrocalcinosis, subnephrotic proteinuria and chronic kidney disease are also known to occur.[4,5] Though distal RTA is a common variety, cases of proximal RTA and Fanconi's syndrome in pSS have been described in literature. [6,7] Osteomalacia is a known

complication of RTA, though this complication in the setting of pSS related RTA has not been studied extensively. There are, however, case reports of this complication in pSS including a few from Indian subcontinent.[7-10] Diagnosis of pSS was difficultin our patient as our patient refused biopsy, even, though patient had 3 AEC criteria including positive schimer's test; high titre anti-Ro and anti-La antibody. This case report underscores the importance of evaluating for pSS in patients with RTA, hypokalemic paralysis and osteomalacia, even if the patients do not voluntarily complain of sicca symptoms. In this regard, it is notable that hypokalemia is the most common electrolyte abnormality in patients with dRTA. The mechanisms of distal RTA-induced hypokalemia include decreased distal tubular Na delivery, secondary hyperaldosteronism, defective H-K ATPase and bicarbonaturia.[6]

Osteomalacia and osteoporosis is caused by RTA is rarely seen as the presenting feature of Sjogren's syndrome. It is far more common with proximal than distal RTA.

In proximal RTA, renal phosphate loss is the main contributing factor to osteoporosis and osteomalacia,while in distal RTA it is secondary to hypophosphatemia and acidosis and in addition associated vitamin D deficiency may be another contributing factor.

In our patient 25(OH)D3 was normal, osteomalacia was diagnosed by presence of radiological features of osteopenia and presence of looser's zone.

Although hypokalemia is frequent sequel of RTA, a severe symptomatic decrease in serum potassium concentration has been described in a few cases only. Hypokalemic paralysis is a rarely encountered complication of RTA secondary to pSS. Only 18 cases were described between 1966 and 2004.[7] Subsequently, approximately 25 more cases have been reported.[8-10] Here, we present a report of a case that presented to us with hypokalemic paralysis secondary to distal RTA, which on further work up, was found secondary to pSS. our patient did not have any evidence of proximal tubular dysfunction. In conclusion, the kidney involvement in pSS can uncommonly present as hypokalemic paralysis and osteomalacia in the absence of significant sicca symptoms or may precede sicca symptoms. Sjögren's Syndrome should be investigated in any patient presenting with recurrent hypokalemic paralysis from RTA, even in the absence of the sicca syndrome.

Limitation

Renal biopsy and salivary gland biopsy couldn't perform as patient denied.

Conclusions

Renal tubular acidosis has been identified to lead to osteomalacia in adults. Bone involvement is more frequent in proximal RTA (Type 2) but distal RTA (Type 1) can also cause osteomalacia and osteoporosis due to loss of calcium salts from bone and hypophosphatemia. Our case is rare, unique and interesting because in spite of the rarity of osteoporosis revealing Sjogren's syndrome, this complication should be taken into consideration by physicians in the diagnosis of Sjogren's syndrome with renal tubular acidosis. Latent renal tubular disease is quite prevalent in Sjogren's syndrome, but is infrequently complicated by osteoporosis. Primary Sjogren's syndrome could be a differential diagnosis in patients with muscular weakness, recurrent hypokalemia and osteoporosis and osteomalacia.

Recommendation

Hypokalaemic periodic paralysis need through evaluation as it may be the initial presentation of primary Sjogren Syndrome complicated with distal RTA.

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Contribution of authors

IJ- Drafting, citing references & final approval.
MHA-Design, critical revision & final approval.

Disclosure

Both the authors declared no conflict of interest.

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