International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Sjogren's Syndrome Presenting as Hypokalemic Periodic Paralysis

Dr. Manjiri Naik[1], Dr. Siddhraj Vinod Paramshetti[2], Dr. Sushen Ghadge[3], Dr. Shubham Patel[4], Dr. Kartik Doshi[5], Dr. Abhay Bhosale[6], Dr. Kahaan Shah[7]

[1]Professor & Head Department of Medicine, MGM Medical College, Aurangabad

[2]Chief Resident, Department of Medicine, MGM Medical College, Aurangabad

[3]Associate Professor, Department of Medicine, MGM Medical College, Aurangabad

[4]Chief Resident, Department of Medicine, MGM Medical College, Aurangabad

[5]Junior Resident, Department of Medicine, MGM Medical College, Aurangabad

[6]Junior Resident, Department of Medicine, MGM Medical College, Aurangabad

[7]Junior Resident, Department of Medicine, MGM Medical College, Aurangabad

Abstract: ***Sjogren's syndrome is a prototype autoimmune disease characterised by lymphocytic infiltration of the exocrine glands resulting in xerostomia, dry eyes, and profound B-cell hyperactivity. The syndrome has unique features since it presents with a wide clinical spectrum from organ-specific to systemic disease; can occur alone or in association with other systemic rheumatic diseases. Distal renal tubular acidosis is a known cause of hypokalemia, which may rarely be severe enough to present as hypokalemic paralysis. Sjogren's syndrome presenting for the first time with hypokalemic paralysis due to dRTA in a patient with no sicca symptoms is even rarer. The only evidence of underlying Sjogren's syndrome in our patient was positive serology and evidence of RTA. Case report:36 year, Female not a known case of any comorbidities presented with sudden onset proximal muscles weakness of all four limbs in one day. No history of fever, diarrhoea, steroid or diuretic use, animal bite or dry eyes or joint pain. There was no sensory or autonomic involvement. On examination she was vitally stable with areflexic quadriparesis with no cranial nerves involved. Lab wise potassium was 2.6 with arterial blood gas analysis suggestive of metabolic acidosis and trans-tubular potassium gradient of suggestive of renal loss probably Distal RTA. ESR and CRP-q being normal with no ongoing inflammatory pathology. ANA by IF was sent which was 1:1000 with Speckled pattern. ANA Blot was sent which was strong positive for SSA, SSB and Ro52kD establishing a diagnosis of Sjogren's disease. She received potassium correction and oral sodium bicarbonate and currently on lifelong potassium without development of any sicca symptoms or joint involvement till as of date. Conclusion: Sjogren's syndrome, a connective tissue disorder related to impaired exocrine gland involvement and late onset joint involvement rarely presents as Hypokalemic periodic paralysis. Thus, it is paramount for clinicians to remember to rule out Sjogren's syndrome in case of hypokalemic periodic paralysis in middle age female group even in absence of sicca symptoms.***

Keywords: Sjogren's disease, hypokalemiac periodic paralysis, distal rta, hypokalemia, SSA, SSB, Shohl's.

1. Introduction

Sjogren's syndrome (SS) is a chronic autoimmune exocrinopathy characterized by lymphocytic infiltration of lacrimal, salivary, and other exocrine glands. Sjogren's syndrome derives its name from Henrik Sjogren, who introduced the term "keratoconjunctivitis sicca" for dryness of eyes noted in patients. Systemic features of Sjogren's remain to be multisystemic.

Hypokalemic periodic paralysis,a channelopathy, caused by the skeletal muscle ion channel mutations, most commonly calcium channel and less commonly the sodium channels. The patients present with sudden onset of focal flaccid paralysis or generalized paralysis associated with hypokalemia, which persists for several hours to resolve with correction.

Renal tubular acidosis (RTA) clusters a group of disorders characterized by the inability of different segments of the renal tubule to handle bicarbonate reabsorption and/or non-volatile acid secretion thus causing impaired acid–base homeostasis. According to their pathophysiological basis, four types of RTA are typified. Distal RTA (dRTA), also called type 1 RTA, is a rare genetic disorder characterized by the inability of the distal nephron to maximally increase the urinary secretion of protons (H +) in the presence of metabolic acidosis.

Hence Sjogren's presenting with Distal RTA is rare and of which Hypokalemia being the only presenting feature is ever rarer.

2. Case Report

A 41-year-old woman presented to the Emergency Department (ED) with the history of weakness of both lower limbs for two days that was preceded by muscle cramps of three days duration. Her weakness was insidious in onset and gradually progressive in nature affecting the upper limbs by next day with no history of altered sensorium, seizure and bladder or bowel involvement. Her past medical history was positive for repeated hospital admissions following episodes of weakness and fatigue associated with hypokalaemia for the past three years which was managed in the line of hypokalemic periodic paralysis that responded well to

supplemental potassium alone. She denied history of vomiting and intake of diuretics, alcohol, or laxatives. Previous medical records revealed negative results for antibody against acetylcholine receptor that ruled out myasthenia gravis. No history of joint pain, dry skin, alopecia, rash, palpitations, weight gain or weight loss, sweating was noted.

On physical examination, vital signs were within normal limits with higher mental functions intact. On Central nervous system examination, Power in lower limbs and upper limbs was 2/5 and 3/5 respectively affecting both proximal and distal group of muscles. Superficial and Deep Tendon reflex where absent with plantar being mute. No sensory or autonomic involvement was present with cranial nerves being spared. Cardiovascular, respiratory, gastrointestinal and thyroid examination findings being normal. ECG was done which had ST T flattening. Arterial Blood Gas Analysis was sent in ED assuming be HPP, which revealed K of 2.8 with Normal Anion Gap Metabolic Acidosis. Patient was evaluated for the cause of hypokalemia and the TTKG was summed up to 5 which summed up to Renal Potassium Wasting.

Patients Potassium was corrected via intravenous route @ 10cc/hr via central line. In via of finding the cause of Distal RTA ANA was sent which was 1:320 Centromere pattern. Further ANA Blot was sent which was positive for Anti SSA, Anti SSB and Ro52kd were positive. Hence a diagnosis of Sjogren's was made in absence of all its primary feature.

Table 1: Laboratory findings in case.

Test	Value	Test	Value
SERUM K	2.8mEq/L	TSH	2.75 mIU/ml
SERUM NA	142mEq/L	PH	7.260
URINE K	33.80 mmol/l	HCO3-	17.50 mmol/L
SERUM OSMOLARITY	295.80 mosm/kg	ANION GAP	8.90mmol/L
URINE OSMOLARITY	895 mosm/kg	URINE PH	7.50

Table 2: ANA Blot report, representing Ro 52kD, SSA, SSB strongly positive suggestive of Sjogren's Syndrome

	Observed Value	Reference Range	Disease association
Mi-2ß	Negative,2	Negative	Polymyositis and Dermatomyositis
Ku	Negative,1	Negative	SLE, Sjogren's syndrome, scleroderma, Myositis & MCTD
Sm/RNP	Negative,3	Negative	MCTD, Sharp syndrome
Sm	Negative,0	Negative	SLE
SSA	**Strong Positive,107**	Negative	Sjogren syndrome
Ro 52kD	**Strong Positive,135**	Negative	AutoImmune (Sjogren syndrome) & Infectious diseases.
SSB	**Strong Positive,71**	Negative	Sjogren syndrome, SLE
Scl-70	Negative,1	Negative	Systemic sclerosis
PM-Scl 100	Negative,1	Negative	Overlap syndrome (polymyositis,Dermatomyositis & systemic sclerosis)
Jo-1	Negative,1	Negative	Polymyositis, Interstitial lung fibrosis
CENP-A/B	Negative,1	Negative	CREST syndrome
PCNA	Negative,1	Negative	SLE
dsDNA	Negative,1	Negative	SLE
Nucleosome	Negative,0	Negative	SLE
Histones	Negative,0	Negative	Drug induced lupus, Rheumatoid arthritis
Ribosome PO	Negative,2	Negative	SLE
AMA M2	Negative,2	Negative	Primary biliary cirrhosis

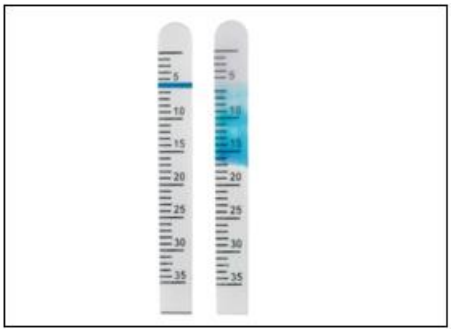

Figure 1: Schiermer test depicting normal values

3. Discussion

Primary Sjogren's disease is a chronic multisystem inflammatory disorder characterized by lymphocytic infiltration of the lacrimal and salivary glands and resultant dry eyes and mouth. A variety of other disease manifestations may also be present, including additional issues with sicca, such as dryness of the skin, nasal passages, and vagina; extraglandular involvement; and systemic symptoms, such as fever and malaise (1-4).

Primary Sjogren's disease is typically associated with a lymphocytic and plasmacytic infiltrate in the salivary,

parotid, and lacrimal glands, leading to a sicca syndrome. This immune process can also affect nonexocrine organs, including the kidneys, producing a tubulointerstitial nephritis and defects in tubular function. Less commonly, a variety of glomerular diseases may also occur in association with Sjogren's disease. The reported prevalence of kidney involvement in Sjogren's disease varies widely, ranging from 1 to 33 percent [1-4]. Most studies observed kidney manifestations in approximately 5 to 14 percent of patients with Primary Sjogren's disease [4].

The most common manifestations are interstitial nephritis and cryoglobulinemia-related membranoproliferative glomerulonephritis (MPGN) [5,6,7]. The defects in renal tubular function that lead to acid-base and electrolyte abnormalities in patients with Sjogren's disease (most commonly distal renal tubular acidosis [RTA], arginine vasopressin resistance [previously called nephrogenic diabetes insipidus], and hypokalemia) generally occur in conjunction with tubulointerstitial nephritis [3,5,8]; however, the precise mechanisms by which tubular inflammation/injury in Primary Sjogren's disease may lead to specific impairments in tubular function are incompletely understood.

Hypokalemic periodic paralysis can have various aetiologies, prerenal or renal. Taking into consideration the natural course of disease and by measuring urinary potassium levels and by calculating trans-tubular potassium gradient we can run to a conclusion of what the cause can be. Of all causes, RTA leading to hypokalemia is rare and Sjogrens with RTA is still rarer.

Distal RTA (Type 1 RTA) mostly due to H^+ ATPase or H^+K^+ATPase defect. This defect leads to severe acidosis due to failure of the distal tubular cells to excrete H^+ ions in the urine. Hence Urine is alkaline here, with Urinary pH >5.5. Severe acidosis cause calcium resorption from bone causing hypercalcemia, hypercalciuria, nephrocalcinosis (due to hypercalcemia and hyppocitraturia). NH_4Cl loading test was used prior to confirm RTA, failure to cause a fall in urinary pH<5.5 even after loading NH4Cl for 3 days confirmed distal RTA.

Hypokalemia is severe enough in these cases to cause significant paralysis and severe respiratory depression. Correction of potassium through central line is advised at rate of not more than 10mEq/h and not more than 240mEq/day. Oral potassium chloride solution, 15ml contains 20mEq potassium and potassium citrate 5ml containing 10mEq of potassium.

Shohl's solution is the alkali used in the treatment of RTA. It contains sodium citrate 500mg in 5ml and citric acid 640mg in 5ml. 1ml of Shohl's Solution contains 1Meq of citrate or bicarbonate.

Hence, a female patient with 20 to 60 years age group, presenting with acute onset paraplegia, secondary to hypokalemia where all other causes of hypokalemia have been ruled of and has acidosis with renal potassium wasting with positive urinary anion gap and urine dipstick positive for calcium, this patient should be ruled out for RTA and Sjogrens as a differential should be kept in mind being the most important inheritable cause of Distal RTA

References

[1] Saraux A, Pers JO, Devauchelle-Pensec V. Treatment of primary Sjögren syndrome. Nat Rev Rheumatol. 2016 Aug;12(8):456-71. doi: 10.1038/nrrheum.2016.100. Epub 2016 Jul 14. PMID: 27411907.

[2] Ramos-Casals M, Brito-Zerón P, Bombardieri S, Bootsma H, De Vita S, Dörner T, Fisher BA, Gottenberg JE, Hernandez-Molina G, Kocher A, Kostov B, Kruize AA, Mandl T, Ng WF, Retamozo S, Seror R, Shoenfeld Y, Sisó-Almirall A, Tzioufas AG, Vitali C, Bowman S, Mariette X; EULAR-Sjögren Syndrome Task Force Group. EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies. Ann Rheum Dis. 2020 Jan;79(1):3-18. doi: 10.1136/annrheumdis-2019-216114. Epub 2019 Oct 31. PMID: 31672775.

[3] Sumida T, Azuma N, Moriyama M, Takahashi H, Asashima H, Honda F, Abe S, Ono Y, Hirota T, Hirata S, Tanaka Y, Shimizu T, Nakamura H, Kawakami A, Sano H, Ogawa Y, Tsubota K, Ryo K, Saito I, Tanaka A, Nakamura S, Takamura E, Tanaka M, Suzuki K, Takeuchi T, Yamakawa N, Mimori T, Ohta A, Nishiyama S, Yoshihara T, Suzuki Y, Kawano M, Tomiita M, Tsuboi H. Clinical practice guideline for Sjögren's syndrome 2017. Mod Rheumatol. 2018 May;28(3):383-408. doi: 10.1080/14397595.2018.1438093. Epub 2018 Mar 13. PMID: 29409370.

[4] François H, Mariette X. Renal involvement in primary Sjögren syndrome. Nat Rev Nephrol. 2016 Feb;12(2):82-93. doi: 10.1038/nrneph.2015.174. Epub 2015 Nov 16. PMID: 26568188.

[5] Goules AV, Tatouli IP, Moutsopoulos HM, Tzioufas AG. Clinically significant renal involvement in primary Sjögren's syndrome: clinical presentation and outcome. Arthritis Rheum. 2013 Nov;65(11):2945-53. doi: 10.1002/art.38100. PMID: 24166794.

[6] Kidder D, Rutherford E, Kipgen D, Fleming S, Geddes C, Stewart GA. Kidney biopsy findings in primary Sjögren syndrome. Nephrol Dial Transplant. 2015 Aug;30(8):1363-9. doi: 10.1093/ndt/gfv042. Epub 2015 Mar 27. PMID: 25817222.

[7] Jasiek M, Karras A, Le Guern V, Krastinova E, Mesbah R, Faguer S, Jourde-Chiche N, Fauchais AL, Chiche L, Dernis E, Moulis G, Fraison JB, Lazaro E, Jullien P, Hachulla E, Le Quellec A, Rémy P, Hummel A, Costedoat-Chalumeau N, Ronco P, Vanhille P, Meas-Yedid V, Cordonnier C, Ferlicot S, Daniel L, Seror R, Mariette X, Thervet E, François H, Terrier B. A multicentre study of 95 biopsy-proven cases of renal disease in primary Sjögren's syndrome. Rheumatology (Oxford). 2017 Mar 1;56(3):362-370. doi: 10.1093/rheumatology/kew376. PMID: 27940588.

[8] SHEARN MA, TU WH. NEPHROGENIC DIABETIC INSIPIDUS AND OTHER DEFECTS OF RENAL TUBULAR FUNCTION IN SJOERGREN'S

SYNDROME. Am J Med. 1965 Aug;39:312-8. doi: 10.1016/0002-9343(65)90057-4. PMID: 14320699.