

CASE REPORT

HYPOKALEMIC PARALYSIS AND RENAL TUBULAR ACIDOSIS: INITIAL PRESENTATION OF SJOGREN'S SYNDROME

Tania Tofail¹, Sharmin Jahan², Mohd. Abul Hasnat³

Abstract:

Sjogren's syndrome is a rare autoimmune disease affecting multiple systems with varying clinical features. We report a case of 37 year old woman who presented with recurrent episodes of quadriparesis which was attributable to hypokalemia and initially labelled as hypokalemic periodic paralysis. Later on she was found to have metabolic acidosis rather than alkalosis which pointed towards the diagnosis of renal tubular acidosis (RTA) in the absence of apparent gastrointestinal tract loss. Once the diagnosis of RTA was established, an attempt to search the aetiology revealed that she was having primary Sjogren's syndrome (pSS) though she did not have any symptom at the time of diagnosis. She was found positive for anti-SSA. Lip biopsy revealed lymphocytic infiltration in periductal as well as parenchymal region. Schirmer test confirmed presence of severe dry eye. A concomitant existence of autoimmune hypothyroidism was a noteworthy association. She responded well with potassium supplementation and symptomatic treatment. Presentation of this case reminds the importance of vigilance while managing a case of recurrent hypokalemia which might be a rare presenting feature of pSS.

Key words: Primary Sjogren's, Distal renal tubular acidosis, Hypokalemic paralysis

Received: 23.4.2021

Accepted: 28.5.2021

DOI: <https://doi.org/10.3329/bjm.v32i2.53800>

Citation: Tofail T, Jahan S, Hasnat MA. Hypokalemic paralysis and renal tubular acidosis: Initial presentation of Sjogren's syndrome. *Bangladesh J Medicine* 2021; 32: 145-148.

Introduction:

Sjogren's syndrome is a rare autoimmune disorder characterized by chronic inflammation of exocrine glands like salivary and lacrimal glands leading to dry mouth and dry eyes. It has an estimated prevalence of 0.3 to 1 per 1000 population that peaks at 50 years of age with a female preponderance having female: male ratio of 9:1.¹ However it poses a challenge to clinicians when the syndrome presents with extra glandular manifestations in the absence of typical sicca syndrome. Among the non-exocrine glands in <10% cases kidney is affected while tubule interstitial nephritis (TIN) is the most common form of involvement.² TIN can affect all segments of nephron resulting in tubular dysfunctions like renal tubular acidosis and rarely hypokalemic paralysis.³

We present a 37 year old female who presented with recurrent hypokalaemic periodic paralysis as a

consequence of renal tubular acidosis without typical features where further workup lead to a diagnosis of primary Sjogren's syndrome.

Case Report:

A 37 year old normotensive, non-diabetic female came to the outpatient department of our hospital for follow up of her primary hypothyroidism which she had been diagnosed for last 25 years. She was not compliant with her medications recently and complained of fatigue, weakness and somnolence. Apart from adjusting her levothyroxine replacement dosage while reviewing her reports it was found that she had recurrent history of hypokalemia along with development of quadriparesis. She was also found to be unusually short (137 cm, <-5 SD) considering the onset of her hypothyroidism could not explain the presentation. So she was admitted for further evaluation. The patient gave history of recurrent episodes of weakness of all four limbs for last two years

1. Resident, Department of Endocrinology, BSMMU, Dhaka, Bangladesh.

2. Assistant Professor, Department of Endocrinology, BSMMU, Dhaka, Bangladesh

3. Professor, Department of Endocrinology, BSMMU, Dhaka, Bangladesh

Correspondence: Tofail T. Resident, Department of Endocrinology, BSMMU, Dhaka, Bangladesh, E-mail: tania.ali194@gmail.com

which was sudden in onset, symmetrical in nature without any identifiable precipitant e.g. large carbohydrate meal, diarrhea or vomiting. There were no sensory symptoms, respiratory distress, and bladder or bowel involvement. These episodes happened for 7-8 times over this period and she got hospitalized in two occasions where she was found to have hypokalemia. She was treated with oral potassium supplementation and symptoms resolved in 3-5 days. In other occasions she self-treated her with the same medication and improved. There was no history of oral ulcer, joint pain or swelling, rash, polyuria, fever, abdominal pain and weight gain. There was no family history of such illness. She was taking Tab. Levothyroxine 125 microgram daily, episodic oral potassium supplementation. She denied history of diuretic or steroid intake. Her menstrual cycles were regular.

On examination, she was underweight (37 kg), height: 137 cm, BMI-19.7 kg/m², BP-100/70 mm Hg, pulse - 80/min, Respiratory rate- 26 breaths/ min, thyroid gland was not palpable. Her nervous system examination revealed normal higher psychic function, muscle tone- normal, power- 4/5, and no sensory abnormality and flexor plantar response. Other systemic examination revealed no abnormalities.

During the period of hypokalemia (K⁺- 2.5 mmol/l) her ECG showed u wave and prolongation of QRS complexes. Arterial blood gas analysis showed metabolic acidosis with respiratory compensation. (pH-7.42, pCO₂-17.1 mmHg, HCO₃⁻-11.2 mmol/l) and serum electrolytes revealed hyperchloremic hypokalemic non-anion-gap metabolic acidosis. (sodium- 138 mmol/L, potassium- 2.5 mmol/L, chloride- 116 mmol/L, T-CO₂- 13.1 mmol/L).

In the face of metabolic acidosis urine was alkaline (pH-7.00) and specific gravity was 1.012. 24 hours urinary K⁺ - 21.37mmol/l (urine volume-1250ml/24 hrs.). Therefore, a diagnosis of distal RTA was made.

For evaluation of the etiology of distal RTA we performed autoantibody screen. Anti-SSA (Ro) 1.90U/ml (positive >1), Anti-SSB (La) 0.45 U/ml (negative <0.95), RA-63.4 IU/ml (normal <15 IU/ml), ANA- negative. Features were suggestive of primary Sjogren's syndrome. In accordance with the consultation of rheumatologist patient was sent for lip biopsy and schirmer's test. Schirmer's test results was 3 mm both eyes which is consistent with severe dry eye. Histopathology of lip revealed lymphocytic infiltrations in the periductal as well as parenchymal region (Fig.-1).

In addition to her levothyroxine replacement, she is now on oral potassium and bicarbonate supplements,

artificial tear drop, and lifestyle modification to maintain dental and oral hygiene.

Though the patient had no features of sicca syndrome during her initial presentation, now the symptoms are ensuing even with supportive treatment. Patient is euthyroid now with supplementation and hypokalemia is now resolved.

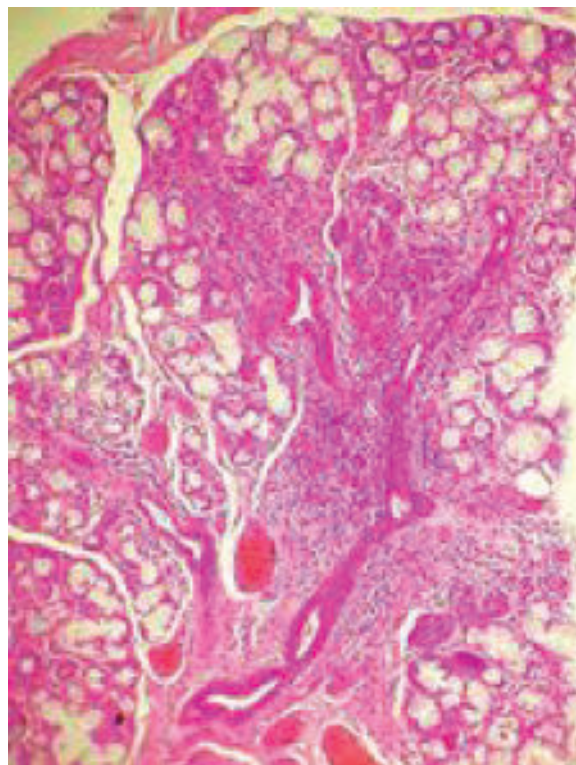


Fig.-1: This slide have lymphocytic infiltrations in the periductal as well as parenchymal regions.

Discussion:

Our patient had history of recurrent severe hypokalemia which was treated as hypokalemic periodic paralysis. An important clue in her diagnostic workup was the presence of metabolic acidosis. Hypokalemia associated with non-anion gap metabolic acidosis and hyperchloremia in the absence of apparent gastrointestinal loss points towards the diagnosis of RTA. Then alkaline urinary pH despite metabolic acidosis established the diagnosis. Renal loss of potassium as a result of tubular dysfunction was also biochemically proven. Hence, a composite diagnosis of recurrent hypokalemia with non-anion gap metabolic acidosis due to distal RTA was reached. The next question to be answered was what the aetiology of this seemingly idiopathic RTA is. The patient had no systemic symptoms or dry eyes or dry mouth. Still we opted for autoantibody screening which came out to be positive. To establish the diagnosis of primary

SS we then performed lip biopsy and schirmer's test both of which yield positive result.

Sjogren's syndrome is an autoimmune condition characterized by abnormal lymphocytic infiltration to exocrine glands like salivary and lacrimal glands caused by autoantigens Ro/SSA and La/SSB resulting in sicca syndrome.⁴ It may occur primarily or secondary to other inflammatory conditions like rheumatoid arthritis. Clinical manifestations are not limited to dry eyes or dry mouth only. Non exocrine organs are affected in varying degree ranging from 30-40%.⁵

The exact prevalence of renal involvement in pSS is yet to be determined. However, the most common involvement in this context is TIN. TIN can affect all segments of nephron, resulting in different forms of tubular dysfunction. Apart from RTA and hypokalemia, Fanconi syndrome, Gittleman syndrome, diabetes insipidus might occur.² Hypokalemia is the most common electrolyte abnormality in patients with distal RTA. The causes of hypokalemia include decreased distal tubular Na⁺ delivery, secondary hyperaldosteronism, defective H⁺-K⁺ ATPase, and bicarbonaturia. Hypokalemic paralysis seen in SS is rare and may sometimes mimic hypokalemic periodic paralysis which is evident in our case.

The diagnosis of Sjögren's presents a challenge to clinicians, particularly when the initial presentation differs from the exocrine manifestation of dry eyes and mouth. The American-European Consensus Classification Criteria has recently revised classification criteria for diagnosis of Sjogren's syndrome that requires four of six criteria, including: ocular or oral symptoms, objective ocular or oral signs, histopathology from a lip biopsy and the presence of autoantibodies.⁶ Our patient did not have subjective symptoms of sicca syndrome but she had evidence of severe dry eye on schirmer's test and lip biopsy from minor salivary gland illustrated diffuse lymphocyte infiltrations. She was positive for autoantibodies too. Thus she fulfilled the criteria of Sjogren's syndrome.

One important feature of our case is coexistence of autoimmune thyroid disease and pSS. This association has been reported in the literature often ranging between 10 to 30%.⁷⁻⁹ A recent meta-analysis also found increased risk of thyroid disorder in patients with pSS.¹⁰ Whether they should be considered as manifestations of same pathophysiologic mechanism or polyautoimmunity is not settled yet. Both pSS and AITD are linked with increased risk of development of

lymphoma.¹¹ Thus, this association might significantly influence long term morbidity or outcome in such patients.

Management of pSS is tailored to individual patients' symptoms. Our patient presented with severe hypokalemia which was managed with IV and oral supplementation. Muscarinic agonists are used to stimulate residual salivary gland function and artificial tear drops to alleviate dry eyes.¹¹ In case of marked systemic features corticosteroids, hydroxychloroquine and methotrexate are used. Biologics like Rituximab is reserved for disabling systemic symptoms despite use of DMARDs.¹² At present there is no cure. Our patient responded well to potassium supplementation and other lifestyle measures. Over the last 2 years follow up she did not have any further attack of severe hypokalemia. So far, she has not required any systemic agents.

Conclusions:

Although Sjogren's syndrome characteristically present with sicca syndrome it might present with extra glandular manifestations prior to the onset of classical symptoms. Therefore, in seemingly idiopathic RTA cases investigations to elucidate such causes should be carried out. Hypokalemia associated with metabolic acidosis should trigger such suspicion.

Conflict of Interests:

The authors stated that there is no conflict of interest in this article.

Funding:

No specific funding was received for this article.

References:

1. Qin B, Wang J, Yang Z, et al. Epidemiology of primary Sjögren's syndrome: A systematic review and meta-analysis. *Ann Rheum Dis.* 2015;74(11):1983-1989. <https://doi-org.libus.csd.mu.edu/10.1136/annrheumdis-2014-205375> PMID:24938285
2. François H, Mariette X. Renal involvement in Sjögren's syndrome. *Nephrol Ther.* 2020;16(7):440-452. <https://doi-org.libus.csd.mu.edu/10.1016/j.nephro.2020.10.002> PMID:33208269.
3. Yilmaz H, Kaya M, Özbek M, Üreten K, Safa Yildirim I. Hypokalemic periodic paralysis in Sjogren's syndrome secondary to distal renal tubular acidosis. *Rheumatol Int.* 2013;33(7):1879-1882. <https://doi-org.libus.csd.mu.edu/10.1007/s00296-011-2322-z>. PMID: 22212410
4. Brito-Zerón P, Baldini C, Bootsma H, et al. Sjögren syndrome. *Nat Rev Dis Prim.* 2016;2. <https://doi->

- org.libus.csd.mu.edu/10.1038/nrdp.2016.47. PMID:27383445
5. Retamozo S, Brito-Zeron P, Zeher M, Kathy L, Seror R. Epidemiologic subsets drive a differentiated clinical and immunological presentation of primary Sjögren syndrome: Analysis of 9302 patients from the Big Data. Published online 2017. Accessed January 1, 2021. <https://hal.archives-ouvertes.fr/hal-01682664/>
 6. Shiboski CH, Shiboski SC, Seror R, et al. 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjögren's Syndrome: A Consensus and Data-Driven Methodology Involving Three International Patient Cohorts. *Arthritis Rheumatol.* 2017;69(1):35-45. <https://doi-org.libus.csd.mu.edu/10.1002/art.39859>. PMID:27785888 PMCid:PMC5650478.
 7. Baldini C, Ferro F, Mosca M, Fallahi P, Antonelli A. The association of Sjögren syndrome and autoimmune thyroid disorders. *Front Endocrinol (Lausanne).* 2018;9. <https://doi-org.libus.csd.mu.edu/10.3389/fendo.2018.00121>. PMID:29666604 PMCid:PMC5891591.
 8. Anaya JM, Restrepo-Jiménez P, Rodríguez Y, et al. Sjögren's Syndrome and Autoimmune Thyroid Disease: Two Sides of the Same Coin. *Clin Rev Allergy Immunol.* 2019;56(3):362-374. <https://doi-org.libus.csd.mu.edu/10.1007/s12016-018-8709-9>. PMID:30187363
 9. Jara LJ, Navarro C, Brito-Zerón MDP, García-Carrasco M, Escárcega RO, Ramos-Casals M. Thyroid disease in Sjögren's syndrome. *Clin Rheumatol.* 2007;26(10):1601-1606. doi:10.1007/s10067-007-0638-6. <https://doi-org.libus.csd.mu.edu/10.1007/s10067-007-0638-6>. PMID:17558463
 10. Sun X, Lu L, Li Y, Yang R, Shan L, Wang Y. Increased risk of thyroid disease in patients with Sjogren's syndrome: A systematic review and meta-analysis. *PeerJ*;2019(3). <https://doi-org.libus.csd.mu.edu/10.7717/peerj.6737>. PMID:30918763 PMCid:PMC6430100
 11. Teixeira Mendes LS, Wotherspoon A. Marginal zone lymphoma: Associated autoimmunity and auto-immune disorders. *Best Pract Res Clin Haematol.* 2017;30(1-2):65-76. <https://doi-org.libus.csd.mu.edu/10.1016/j.beha.2016.07.006> PMID:28288719
 12. Saraux A, Pers JO, Devauchelle-Pensec V. Treatment of primary Sjögren syndrome. *Nat Rev Rheumatol.* 2016;12(8):456-471. <https://doi-org.libus.csd.mu.edu/10.1038/nrrheum.2016.100> PMID:27411907.