Diabetes Mellitus and Renal Tubular Acidosis in Primary Sjögren’s Syndrome

E Benjamin Samraj Prakash*, James Jerene Jayanth*, M Edwin Fernando**

Abstract

Sjögren's syndrome is an autoimmune disease with multisystem involvement characterised by lymphocytic infiltration of exocrine glands resulting in keratoconjunctivitis sicca, xerostomia and bilateral parotid gland enlargement. Renal manifestation is characteristically chronic lymphocytic tubulointerstitial nephritis. Diabetes mellitus in Sjögren’s syndrome has also been described in literature. In this article we discuss two cases of Sjögren’s syndrome with diabetes mellitus and renal manifestations.

Introduction

Sjögren's syndrome is characterised by dry mouth (xerostomia), dry eyes (keratoconjunctivitis sicca) and bilateral parotid enlargement. About a third of patients have extraglandular manifestations which include arthritis, vasculitis, Raynaud's phenomenon, renal involvement and lymphoma. The incidence of diabetes mellitus (DM) in Sjögren’s syndrome was about 4.1%2 in previous studies. Following the case published in these columns,1 we managed 2 more cases of primary Sjögren’s syndrome with renal tubular acidosis (RTA). Both these patients had type 2 DM in addition to renal involvement.

Case Report 1

A 50 year old female was admitted with weakness of both upper and lower limbs for 1 day. There were no sensory symptoms or H/O bowel and bladder involvement. No H/O joint pains or dryness of eyes. She was not a known diabetic or hypertensive.

On examination, she was conscious and afebrile. Cranial nerves were normal. The muscle power was grade 3/5 in both the upper limbs and 2/5 in the lower limbs. Deep tendon reflexes were elicitable and plantars bilaterally flexor. Examination of the cardiovascular and respiratory system was unremarkable.

Her white blood count was 11,700 cells/cumm, Hb-13.8gms, ESR-45mm/hr, sodium-142 mEq/L, potassium-1.9 mEq/L, chloride-110 mEq/L, bicarbonate-22 mEq/L. Urinary potassium excretion was 700 mEq/day, 24 hours urinary protein was 1530 mg for 24hrs (40-120mg). ABG showed metabolic acidosis with respiratory compensation (pH-7.290, PaCO₂-18.9 mmHg, PaO₂-124.3 mmHg). Hyperchloremic metabolic acidosis with normal serum anion gap suggested the diagnosis of renal tubular acidosis. This was confirmed by a positive urine anion gap. Urinary pH of 6 with hypokalemic confirmed distal (type 1)

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*Consultant Physician, **Consultant Nephrologist, C.S.I. Kalyani Multispeciality Hospital, 15, Dr. Radhakrishnan Salai, Mylapore, Chennai 600 004.
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renal tubular acidosis.

Schirmer’s test was positive and SS-A (Anti-Ro) and SS-B (Anti-La) was positive. RA factor was 82 IU/ml (<25-Normal), ANA-3.8 OD index (<1 OD index – normal). Labial salivary gland biopsy revealed lymphocytic infiltrate with focal lymphoid follicle formation (Fig. 1). A diagnosis of primary Sjögren’s syndrome with distal (type 1) renal tubular acidosis with hypokalemic paralysis was made.

She was treated with steroids (prednisolone 1 mg/kg/day), potassium chloride infusion, oral potassium citrate and Shoel's solution. Following this her weakness recovered completely. Patient has been followed up in the OPD with sequential haemograms and ABG analyses for the past 30 months. She was doing well on steroids (prednisolone, dose gradually reduced to 10 mg od) and oral potassium citrate (30 ml/day) for about 18 months. Following this, she gained weight of 4 kgs over 18 months and developed diabetes mellitus (confirmed by GTT after withdrawal of steroids for 1 month) and was changed over to methotrexate (10 mg once weekly), potassium citrate and metformin (500 mg tds). She is doing well for the past 12 months on these drugs without worsening of her symptoms and a HbA1c ranging between 7.5 to 9.5 at different times over this period.

Case Report 2

A 47 year old female, suffering from a chronic slowly progressive arthritis for the past 10 years and diabetes mellitus for the past 7 years was admitted for worsening joint pain. She was receiving methotrexate 7.5 mg once weekly and a sulfonylurea (glimepiride 2 mg od). She gave history of dry eyes and dry mouth for many years and a suspected right parotid gland abscess 2 years back for which incision and drainage had been done (Fig. 2). Examination showed bilateral parotid gland enlargement and chronic joint changes consistent with persistent inflammatory arthritis was seen in both hands (Fig. 3). Schirmer’s test was consistent with Sjögren’s syndrome. She was tachypnoic at rest and examination of other systems was unremarkable.

Her white blood count was 5500 cells/cumm, Hb-7.0gms/dl, ESR-105mm/hr, Na+-131 meq/L, K+-5.4 mEq/L, chloride-103 mEq/L, bicarbonate-23 meq/L. Peripheral smear showed macrocytes with MCV of 95.9 fl. Plasma urea was 28 mg% and creatinine 0.9 mg%. Random blood sugar at admission was 327 mg/dl and urine acetone was negative. HbA1c was 11.5%. ABG showed metabolic acidosis with respiratory compensation (pH-7.238, PaCO2-23.7mm Hg, PaO2-111.4mm of Hg). Urinary anion gap (urine Na+ + urine K+ – urine Cl- = 28.3 + 47.3 – 49.1). Presence of hyperkalemia confirmed type 4 renal tubular acidosis.

SS-A (Anti-Ro) and SS-B (Anti-La) was positive. RA factor was 56 IU/ml (<25-Normal), ANA-0.8 OD index (<1 OD index – normal). Labial salivary gland biopsy showed focal lymphocytic sialoadenitis. A diagnosis of primary Sjögren’s syndrome with methotrexate induced anaemia, diabetes mellitus and type 4 renal tubular acidosis (hyperkalemic distal RTA) was made and she was treated with blood transfusion, methylprednisolone 500 mg IV OD for 3 days followed by oral prednisolone 1 mg/kg/day, Shoel's solution and insulin which was later changed over to oral sulfonylurea (glybenclamide 5 mg bd).

Discussion

The renal manifestations of the case 1 are due to Sjögren’s syndrome as they antedate the onset of DM. However, it is worth noting in this case that it has been possible to prevent hypokalemia and secondary hypokalemic paralysis for over 30 months by use of immunosuppressive drugs and potassium citrate.

Sjögren’s syndrome with type 2 DM and nephrotic syndrome has been reported previously. However, the association of Sjögren’s syndrome with type 2 DM and type 4 RTA seen in case 2 is being reported for the first time to our knowledge.

Even though a causative association between type 1 diabetes mellitus and Sjögren’s syndrome has been suggested such an association may not apply to the type-2-DM seen in these patients. However, a positive Schirmer’s test has been demonstrated in 13.9% of type 1 DM and 38.6% of type 2 DM patients. The proportion of patients with Sjögren’s syndrome developing type 2 DM in recent years needs to be studied.

Type 4 RTA seen in case 2 is well known to occur with diabetic nephropathy. A study of 60 patients with Sjögren’s syndrome did not find type 4 RTA in any of them. However, more studies are needed to determine whether Sjögren’s syndrome contributes to the development of type 4 RTA in the diabetic population particularly those with positive Schirmer’s test. It may also be worth studying whether the incidence of type 4 RTA is more common in this population of diabetics with a positive Schirmer’s test than in other diabetics. Type 1 (hypokalemic distal) RTA in Sjögren’s syndrome may also evolve into a type 4 (hyperkalemic distal) RTA with the onset of diabetic nephropathy. These possibilities need to be evaluated further.

References

4. Binder A, Maddison PJ, Skinner P, Kurtz A, Isenberg DA. Sjögren’s syndrome with type 2 DM and type 4 RTA seen in case 2 is being reported for the first time to our knowledge.