Hypokalaemic Paralysis and Normocalcaemic Tetany – A Rare Presentation of Sjogren’s Syndrome

M Selvaganesh*, A Murali**, RV Mookambika***, K Jayachandran****

Abstract

38 year old woman was admitted with acute onset of quadriplegia. Biochemical investigation revealed severe hypokalaemia with hyperchloraemic metabolic acidosis, alkaline urine, and positive urinary anion gap which are the hallmark of distal tubular acidosis. In addition she also had hypophosphataemia, normoglycaemic glycosuria, aminoaciduria, and hyperphosphaturia suggestive of proximal tubular dysfunction. Further evaluation confirmed the diagnosis of Sjogren’s syndrome. Interestingly our patient also had carpopedal spasm despite normal calcium and magnesium level. Quadriplegia and carpopedal spasm improved with correction of hypokalaemia and acidosis. Proximal tubular abnormalities (except albuminuria) were normalised at the time of discharge. Distal tubular acidosis is a well known renal manifestation of Sjogren’s syndrome. But this type of transient proximal tubular dysfunction with distal tubular acidosis in Sjogren’s syndrome is very rare and hypokalaemic tetany also deserves mention.

Introduction

Sjogren’s syndrome is a systemic autoimmune disorder primarily affecting exocrine glands occurring either alone (primary) or in association with other autoimmune disorders. Even though it primarily affects salivary and lacrimal glands, extra glandular manifestations were reported in 1/3 of the patients and can precede the sicca symptoms.1,2 Overt or latent renal tubular dysfunction due to autoimmune tubulointerstitial nephritis is a common extra glandular manifestation occurring in up to 25-35% of patients and it presents as distal tubular acidosis or nephrogenic diabetes insipidus.1,3 Proximal tubular abnormalities are less common manifestation.4 Here we report a patient with concomitant distal tubular acidosis (RTA) and transient generalised proximal tubular dysfunction as a presenting manifestation of Sjogren’s syndrome along with normocalcaemic tetany.

Case Report

38 year old female was admitted with acute flaccid quadriplegia without any sensory deficit or meningeal signs. She had no history of trauma or fever. Clinical examination was unremarkable except for the pure motor quadriplegia. She developed carpopedal spasm with positive chvostek’s sign by 2nd hour of admission. Her complete blood count, blood sugar, HbA1C, renal and thyroid function tests were within reference range. Her Vitamin D (24.26 ng/ml) and parathyroid hormone assay (58.7 pg/ml) were within normal limits. Liver function test showed hyperglobulinaemia (Total proteins – 7.8 g/dl, Albumin – 3.0 g/dl and Globulin - 4.8 g/dl). Her serum uric acid was 2.1 mg%. Following was her electrolyte panel: Sodium -142 meq/l, Potassium -1.11 meq/l, Bicarbonate -12 meq/l, Chloride -116 meq/l, Total Calcium – 9.2 mg/dl, Ionized Calcium – 4.8 g/dl, Anion Gap -14 meq, Phosphorus 1.49 mg/dl, Magnesium 2.23 meq/l. Her
arterial blood gas analysis showed compensated metabolic acidosis. Urinalysis disclosed a pH of 6.2, albuminuria (1+) and glycosuria (3+). Her 24 hour urinary protein excretion was 124 mg/day. Her urine spot sodium was normal (96 mEq/l), anion gap [UAG = Spot urine Na+ K- Cl] was +4 (positive) and urine osmolal gap [Measured osmolality (294 mosm/kg) – Calculated osmolality (242 mosm/kg)] was 52 mosm/kg. Her ECG on admission showed sinus rhythm with prominent “u” waves and corrected QT interval was 465 ms. Her Chest X ray, Ultrasonogram of abdomen and MRI of brain and spine were normal.

On analysing, the investigations revealed hypokalaemia, hypophosphataemia, hyperchloraemic normal anion gap metabolic acidosis and hypouricaemia. Urinary finding of positive anion gap (≤10 in the presence of metabolic acidosis), low osmolal gap (< 100 mosm/kg), urine pH > 5.5 and normal urine sodium suggest an intrinsic defect in the distal urinary acidification mechanism. Hypokalaemia with trans tubular potassium gradient (TTKG= [K+ Urine/K+ Plasma] / [Urine Osmolality/Plasma Osmolality]) of 20.4 suggest tubular wasting. These findings confirmed the presence of distal RTA. But she also had normoglycaemic glycosuria, albuminuria, aminoaciduria, hyperphosphaturia [FEP-24% (normal 5-12%)] and hyperuricaciduria [FEUA-37.6% (normal – 10-12%)] suggestive of a proximal tubular dysfunction.

On further evaluation features of sicca syndrome - history of recurrent episodes of parotid swelling, dry mouth and dryness of eye were present in her. Further workup showed positive Shirmer’s test (2 mm in 5 mins) with high titres of anti nuclear, anti Ro and anti La antibodies which is compatible with Sjogren’s syndrome. Viral markers for hepatitis B and C, enzyme linked Immunosorbent assay for Human immunodeficiency virus were negative. The patient was treated with intravenous potassium (160 mEq over 36 hours at a rate of 10 mEq/hour) and bicarbonate replacement. She didn’t receive any phosphorus or calcium. Her serum potassium level was normalised by 2nd day of admission and she had a complete neurological recovery. She didn’t have any carpopedal spasm from 3rd day of admission and “u” waves disappeared in the ECG. Glycosuria was not present from the 3rd day but albuminuria persisted. Serum phosphate level was improved by 3rd day and uric acid level was normalised by 5th day. On 5th day of hospitalisation estimated fractional excretion of phosphate (10%) and uric acid (12%) became normal. Her serum bicarbonate on discharge was 16 meq/l and urine pH was 7.0. Oral prednisolone (40 mg OD) was started on the day of discharge. She was also advised to continue sodium bicarbonate and potassium citrate. During follow up (2 months later) she was having normal serum potassium, phosphate and uric acid but low bicarbonate (15 meq/l). Her urinary pH was 6.6 and FEP, FEUA were within normal range. She neither had glycosuria nor albuminuria. One year after initial presentation she was maintaining her serum bicarbonate around 16 -18 meq/l and potassium level above 3.8 meq/l and her eye symptoms were better with artificial tears.

Discussion

Sjogren’s syndrome (SS) is chronic autoimmune disease due to lymphocytic infiltration of exocrine glands characterised by xerostomia and dry eyes. It can be primary or secondary to other autoimmune disorders. The diagnosis of primary Sjogren’s syndrome in our patient was established based on the revised international criteria for Sjogren’s syndrome (American European Consensus group). The common renal manifestation is distal renal tubular acidosis or nephrogenic diabetes insipidus. Proximal tubular dysfunction is uncommon in Sjogren’s syndrome. Only 10 cases of SS- related generalised proximal tubular dysfunction have been reported till date. All of them had concurrent distal RTA, concentration defect and renal dysfunction except one patient. Our patient also had concomitant distal tubular acidosis and proximal tubular dysfunction; uniquely she had normal renal function and rapid recovery of proximal tubular function within a week (5 days) prior to any immunosuppressant therapy. Available follow up reports of 5 cases showed improvement only after 6 months to 1 year after immunosuppressant therapy. We could explain this rapid recovery of proximal tubular dysfunction in our patient with two hypotheses: 1. Even though it is a chronic inflammatory disorder, intermittent worsening and remission as evidenced clinically by recurrent enlargement of exocrine salivary gland is a characteristic manifestation of Sjogren’s syndrome. Both kidneys and exocrine glands would have similar pathogenesis and it’s reversibility depends on the stage of the disease or treatment. 2. The other possible mechanism is hypokalaemic nephropathy. The duration and reversibility of tubular dysfunction in hypokalaemic nephropathy depends on the pathological changes in the tubules which in turn is determined by the duration and severity of hypokalaemia. Acute severe hypokalaemia can cause intrarenal hypoxia which may result in vacuolar degeneration without any destruction or atrophy of tubules whereas chronic hypokalaemia will produce atrophy of the tubules [milder the pathology sooner the reversal]. Hence in our patient either transient tubulitis or hypokalaemic nephropathy could be the cause for transient proximal tubular dysfunction. Histopathological examination would have shown...
the definitive pathological changes but biopsy was not done because our patient didn’t consent.

Chronic metabolic acidosis can induce reversible hyperphosphaturia and hyperuricosuria will not explain the generalised proximal tubular dysfunction with normoglycaemic glycosuria and aminoaciduria. Even though hyperglobulinaemia was present in LFT, serum protein electrophoresis showed polyclonal hyperglobulinaemia without M band and absence of light chain in the urine ruling out the possibility of hyperglobulinaemia as a cause for proximal tubular dysfunction.

The other important clinical feature of our patient was normocalcaemic tetany. She developed carpopedal spasm (tetany) within 1-2 hrs of admission. Serum ionised calcium, magnesium were normal but she had metabolic acidosis. Carpopedal spasm improved with correction of hypokalaemia. Hypokalaemic (normocalcaemic) tetany is an entity where in patient develop carpopedal spasm despite normal serum ionised calcium and magnesium. Flaccid paralysis is the most common manifestation of hypokalaemia; hence it is paradoxical to have tetany representing neuromuscular irritability in a hypokalaemic patient. There are 2 possible explanations for this paradoxical phenomenon: 1. Intracellular-extracellular potassium ratio (Ki/Ke), and its transmembrane conductance determines neuromuscular excitability, not the extracellular potassium value alone. It has been shown in myocardial cells when the plasma potassium falls below 2.7 mmol/l, resting membrane potential increases due to marked fall in K+ conductance leading to depolarisation rather than hyperpolarisation. Similar mechanism can occur in other muscles resulting in paradoxical irritability and persistent spasm. 2. The other possible explanation may be due to differential effects of hypokalaemia on muscle and peripheral nerves. If hypokalaemia predominantly affects the muscle it produces flaccid paralysis and it causes carpopedal spasm when nervous tissue is affected.

Even after Fourmen’s experiment on human model (half century ago) concretely demonstrated latent tetany with isolated hypokalaemia (normal pH, calcium, magnesium in serum), only very few (<10) clinical case reports of hypokalaemic tetany are available in the literature. But there were other confounding abnormalities like alkalosis and other electrolytes disturbances in those patients except in 2 cases by J. Ault and Jacob. But our patient had hypokalaemic tetany which improved with correction of hypokalaemia and acidosis.

The other important cause for flaccid quadriplegia with hypokalaemia is Familial hypokalaemic Periodic Paralysis (FPP). These two entities have to be differentiated since acetazolamide used in FPP aggravates RTA and sodium bicarbonate used in RTA aggravates hypokalaemic periodic paralysis.

Conclusion

Sjogren’s syndrome can present with concurrent proximal tubular dysfunction and distal RTA but a unique combination of distal RTA and transient proximal tubular dysfunction with normal renal function recovering without any immunosuppressant therapy is not reported previously. In addition the presence of hypokalaemic tetany adds one rarer feature in our patient.

References