Primary Sjogren's syndrome presenting as Acute Flaccid Quadriplegia:

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ABSTRACT

Primary Sjögren's Syndrome presenting as acute flaccid quadriplegia is rare. We present a patient who also developed renal tubular acidosis and further discuss here the management in relation to hypokalemia in the setting of this syndrome.

KEY WORDS: Primary Sjögren's syndrome, Quadriplegia, Renal tubular acidosis, Hypokalemia

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Introduction

Acute flaccid quadriplegia is a common neurological problem. Though most of them are Guillain- Barre syndrome but one has to keep in mind hypokalemia which can mimic the syndrome. Routinely hypokalemia is corrected in the chloride form, whereas in renal tubular acidosis giving potassium as chloride may not be enough and potassium citrate has to be given which is converted to bicarbonate correcting acidosis and the potassium level. Primary Sjögren's Syndrome presenting as acute flaccid quadriplegia is rare. We present a patient who also developed renal tubular acidosis and further discuss here the management in relation to hypokalemia in the setting of acidosis.

Case report

A 30 year female presented with a 24 hour history of pain in both the thighs followed by rapid and progressive weakness of all four limbs. When reviewed at the emergency, the patient was gasping and sustained a respiratory arrest for which she was promptly intubated and shifted to the intensive care unit where she was put on mechanical ventilation. On further inquiry she did not have any preceding history of fever, rash, diarrhea, flu-like symptoms, recent vaccination or joint or muscle pain, photosensitivity or polyuria. There were no prior such episodes and family history was also non-contributory. Significantly, she was a case of primary hypothyroidism for the last 4 years and taking thyroxine supplementation. She had normal menstrual cycles.

Preliminary examination showed vitals of : Pulse=84/min, BP=140/80, Respiratory rate (on SIMV) pO2=99% (FiO2=0.4) Head and neck examination was normal with no thryomegaly, lymphadenopathy or parotid enlargement. Neurological examination showed patient to be conscious and cooperative. Cranial nerves were normal. Pupils bilaterally equal and reacting to light. Motor system evaluation showed normal bulk of the muscles, Grade 0 power in both upper and lower limbs with all deep tendon reflexes being absent. Plantar responses were also absent. Sensory evaluation for pain and crude touch were unremarkable.

Investigations at the time of admission (Table 1) showed severe hypokalemia, mild hyperglycemia, hyperchloremia and normal anion gap metabolic acidosis. Urine analysis showed 1+ albuminuria, urine Albumin Creatinine Ratio was 34. ECG showed ST and T wave depression and U-wave depression. A urine pH of 6.5 in the presence of severe metabolic acidosis suggests the possibility of urinary acidification defect. Given the severity of symptomatic hypokalemia, the possibility of Type1(distal) renal tubular acidosis(RTA) was kept. X-Ray and sonogram of the abdomen were normal. Electromyography (EMG) showed no spontaneous activity and nerve conduction studies of both upper and lower limb showed reduced CMAP, sensory NCS was normal.

Patient was started on KCl infusion through central line at 10meq/hr initially followed by progressive tapering after S.K rose to 3.0meq/L. Intravenous soda bicarbonate was started after S.K >3.5 meq/L. Arterial blood gas (ABG) showed improvement in acidaemia and oral sodium bicarbonate was given after arterial pH rose to 7.30. Improvement in limb movement was seen within 6 hours of starting KCl infusion. With oral potassium chloride the potassium level could not be maintained and thus potassium citrate was given instead which has advantage of ameliorating acidosis as citrate gets converted to bicarbonate and thus helps in raising potassium level. By day 3 she regained power in limbs to 4/5. She was extubated on day 4 and shifted to the ward. The patient was discharged home on day 8 with sodium bicarbonate tablet and potassium citrate oral solution. Investigations at time of discharge are shown in table 1.

Further work-up showed Rheumatoid Factor(IgG) positive, ANA by immunoflourescence (IF) showing 3+ positive. dsDNA antibody titres 11.73 (normal< 55.0), C3 and C4 levels were normal. Hepatitis B, C and HIV serology were negative. A possibility of Primary Sjögren's Syndrome was kept. Further evaluation of clinical history did not reveal any symptoms of xerostomia and/ dryness of eyes. Anti-Ro/SSA was positive at titres of 23.51U/mL (normal range< 3.0 ) and anti-La/SSB was also positive with a titre of 39.06(normal <3.0U/mL) . Lower lip mucosal biopsy for minor salivary glands showed (Figure1) features of focal lymphocytic sialadenitis fulfilling criteria for...
acidosis. In view of mild proteinuria and bland urinary sediments, patient was put on ramipril 2.5 mg/d. Patient was started on oral prednisolone at 50 mg/d for one month followed by slow taper. She was followed for 6months post admission and she is asymptomatic till date. Medications at the time of last follow up included oral potassium citrate solution, ramipril and prednisolone at 10 mg/d. All ethical approvals were obtained.

Discussion

Sjögren's syndrome is a chronic autoimmune disorder affecting many organs predominantly exocrine glands. In most cases Sjögren's is associated with other connective tissue disorder and when it occurs in isolation is known as primary Sjögren's Syndrome (pSS) as reported here. This syndrome is predominantly seen in middle aged women (M:F=1:9). In addition to dry eyes and dry mouth pSS can also cause renal (renal tubular acidosis, nephritis), thyroid (hypothyroidism or thyroiditis), gastrointestinal (atrophy gastritis), pulmonary and liver disease. Renal and thyroid involvement seen in our case. Systemic symptoms like arthralgias, myalgia and fatigue can also be associated. In patient with sicca, parotid enlargement and neurological findings sarcoidosis is often a close differential diagnosis.

Diagnosis of pSS according to the current American European consensus group criteria, requires at least four of the following six items: subjective xerophthalmia, subjective xerostomia, objective test for xerophthalmia, objective evidence of salivary gland dysfunction, presence of either anti-Ro/SSA or anti-La/SSB antibodies and histopathologic criteria for pSS on minor salivary gland biopsy. One of the four criteria must be either positive serology or positive histopathology. As in our case who present with extraglandular involvement without sicca symptoms, a diagnosis of pSS is possible if both a positive serologic test and histologic criteria are met.

The spectrum of neurological disorders associated with pSS is broad. Estimated prevalence of neurological involvement being 0-100% of patient with pSS. Central nervous system disease in pSS may include subtle cognitive changes which may be hard to detect without psychometric testing. Sjögren's syndrome may cause focal brain lesions, which may present as stroke like episode or more gradual. Optic neuritis, focal paraesthesia, brain stem syndrome like internuclear opthalmoplegia or myelopathy can be other features of pSS, in which case the distinction from multiple sclerosis is important. Meninges can get involved with a spectrum of aseptic meningitis. Rarely, seizures can occur. Some patients may have combination of myelopathy and optic neuritis suggesting mimic of Devic's syndrome.

Peripheral nervous system is more common then CNS involvement. Peripheral neuropathy is often the presenting feature. The peripheral manifestations of pSS can be separated into a number of clinical syndromes, but many patients have combination of these. Distal sensory or sensorimotor neuropathy is the most common, sensory neuropathy, painful sensory neuropathy, autonomic neuropathy, trigeminal sensory

### Table 1

| Laboratory parameters | Values on admission | Values at discharge |
|-----------------------|---------------------|---------------------|
| Hemoglobin (g/dL)     | 14.9                | 12.5                |
| TLC (µL)              | 11,400              | 8,200               |
| DLC                   | P78L30E2            | P70L28M2            |
| Platelet count (µL)   | 228,000             | 325,000             |
| PTTK (sec)            | -                   | -                   |
| Blood Urea (mg/dL)    | 16                  | 25                  |
| S.Creatinine (mg/dL)  | 1.3                 | 0.9                 |
| Random plasma glucose (mg/dL) | 189 | 134 |
| S.Na⁺ (meq/L)         | 146                 | 143                 |
| S.K⁺ (meq/L)          | 1.4                 | 4.1                 |
| S. Mg²⁺ (mg/dL)       | 2.4                 | 2.8                 |
| S.Ca²⁺ (mg/dL)        | 8.2                 | 8.4                 |
| S.Cl⁻ (meq/L)         | 125.6               | 120.7               |
| Bilirubin (T) (mg/dL) | 0.63                | 0.8                 |
| AST (IU/L)            | 10                  | 15                  |
| ALT (IU/L)            | 28                  | 20                  |
| S.Albumin (g/dL)      | 3.4                 | 3.8                 |
| S.Globulin (g/dL)     | 3.3                 | 2.5                 |
| S.Creatine Phosphokinase (CPK-MB) (IU/L) | 18 | 20 |
| Arterial Blood Gas    |                     |                     |
| pH                    | 7.17                | 7.38                |
| pCO₂ (mmHg)           | 36                  | 27                  |
| pO₂ (mmHg)            | 133                 | 150                 |
| HCO₃⁻ (meq/l)         | 12.6                | 15.6                |
| SpO₂ (%)              | 98.2                | 99.3                |
| Anion gap             | 9.2                 | 10.8                |
| Urine Analysis        |                     |                     |
| pH                    | 6.5                 | -                   |
| Specific gravity      | 1.020               | -                   |
| Albumin               | 1+                  | -                   |
| Sugar                 | nil                 | -                   |
| WBCs /HPF             | 2-3                 | -                   |
| RBCs /HPF             | 1-2                 | -                   |
| Urine Albumin : creatinine Ratio (mg/g of creatinine) | 34 | - |
| 24 Hr. urinary protein (mg/24hr) | 580 | - |

Sjögren's. Schirmer's test showed both eye wetting of 7-8 mm (negative) and tear break up time was normal. EMG and nerve conduction studies were normal.

A final diagnosis of active Primary Sjögren's syndrome without sicca syndrome was made along with type 1 renal tubular
neuropathy, mononeuritis multiplex or involvement of multiple cranial nerves. Biopsy of an involved peripheral nerve is likely to show epineurial vasculitis. Other neuropathic presentations occasionally found include painful asymmetric sensory neuropathy, proximal radiculoneuropathy, Guillain-Barre syndrome and lower motor neuronopathy.

Renal tubular acidosis (RTA) is the main cause of hypokalemia with normal anion gap metabolic acidosis. The only other differential in the present case could have been acute diarhoea. However, in the present case there was no such history and the presence of a urine pH>5.5 even during severe metabolic acidosis points towards a defect in renal acidification mechanism. Of the different types of RTA associated with hypokalemia the defect may be due to proximal tubular HCO3 wasting (Type 2 RTA) or impaired H+ secretion due to a defect in the H+-ATPase/K+ ATPase (Type 1 RTA). Hypokalemia, though common in both the types of RTA, is severe and symptomatic in Type-1 RTA. Although the gold standard to distinguish the two is a measurement of fractional HCO3 excretion which is typically >20% in Type 2 RTA. Treatment of distal RTA involves oral intake of sodium bicarbonate along with potassium supplementation as citrate in order to keep serum K+ levels normal and serum HCO3 > 18meq/L.

Renal involvement in Primary Sjögren's Syndrome may be seen in as much as 27% of cases, making it a frequent site for extraglandular involvement after the CNS and the peripheral nerves. In a large case series, reduction in urinary concentrating capacity was the most common defect and was observed in 20% of cases. Prevalence of other renal defects included reduction in creatinine clearance (13%), frank distal RTA (5%), hypokalemia (7%), subnephrotic proteinuria(17%) and nephrotic syndrome(3%). Overt clinical syndromes were rare and only a single case of hypokalemic quadriparesis was noted. Interestingly, the authors noted that renal involvement preceded the onset of clinical/subjective sicca syndrome. Renal biopsies in all cases demonstrated tubulointerstitial nephritis with focal or diffuse interstitial lymphocytic infiltrates. Glomerular lesions are rare in Sjögren's syndrome and if present require an exclusion of other overlapping diseases like SLE and Mixed Connective Tissue Disease. While the response of tubulointerstitial nephritis to steroid treatment is debatable, one study noted a remission of RTA with the use of long term low dose glucocorticoid therapy.

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