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Sjögren syndrome presenting with hypopotassemic periodic paralysis due to renal tubular acidosis

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Summary

Background: Sjögren syndrome (SS) is an autoimmune-lymphoproliferative disorder characterized by mononuclear cell infiltration of exocrine glands. Clinically, Sjögren syndrome (SS) has a wide spectrum, varying from autoimmune exocrinopathy to systemic involvement. There have been few cases reporting that primary SS developed with distal renal tubular acidosis clinically.

Case Report: Here, we present a case with primary Sjögren syndrome accompanied by hypopotassemic paralysis due to renal tubular acidosis. Severe hypopotassemia, hyperchloremic metabolic acidosis, alkaline urine and disorder in urinary acidification test were observed in the biochemical examination of the 16-year-old female patient, who had applied to our clinic for extreme loss of muscle force. After the examinations it was determined that the patient had developed Type 1 RTA (distal RTA) due to primary Sjögren syndrome. Potassium and alkaline replacement was made and an immediate total recovery was achieved.

Conclusions: Hypopotassemic paralysis due to primary Sjögren syndrome is a rare but severe disorder that could lead to death if not detected early and cured appropriately. Thus, effective treatment should be immediately initiated in cases where severe hypopotassemia is accompanied by metabolic acidosis, and the cases should also be examined for extraglandular involvement of SS.

key words: **Sjögren syndrome • hypopotassemic paralysis • distal renal tubular acidosis**

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Background

Sjögren syndrome is a slow paced, chronic, systemic and auto-immune disorder characterized with lymphocytic infiltration of exocrine glands. Sjögren syndrome was firstly identified by Mikulicz in 1982, in a patient who had swelling of bilateral parotid glands and lacrimal gland infiltration. Intense cell infiltration was observed in the biopsy of the glands involved [1]. In 1933, Henrik Samuel Conrad Sjögren detected similar clinical and histologic symptoms in 19 cases – 13 of which belonged female patients – suffering from dry eyes and dry mouths, calling it "keratoconjunctivitis sicca" [2]. In 1953, Morgan and Castleman concluded that Sjögren syndrome and Mikulicz disorder were the same entities. In 1980, Talal defined the disorder as auto-immune exocrinopathy; Skopouli and Moutsopoulos defined it as auto-immune epithelitis [3,4].

Sjögren syndrome is mainly accompanied by dryness of mouth and eyes; these 2 symptoms are called sicca symptoms. Sjögren syndrome is defined as primary Sjögren syndrome if there is no other underlying disorder; and as secondary Sjögren syndrome if it is accompanied by another auto-immune collagen tissue disorder. Rheumatoid arthritis, systemic lupus, erythematosus and scleroderma are the most frequent accompanying auto-immune disorders [5].

The prevalence rate of Sjögren syndrome is about 0.5–5%; the female *vs.* male ratio is 9:1. Fifty percent of the cases are primary Sjögren syndrome [6].

Among the extraglandular manifestations of SS, renal tubular acidosis (RTA) is seen in up to 25–30% of cases; it is usually latent and less symptomatic. RTA is detected by a disorder in urinary acidification tests [7]. Renal tubular acidosis (RTA) is characterized by metabolic acidosis due to specific defects in renal tubular hydrogen secretion [8]. Although there is not a common view of the pathogenic mechanisms of distal tubule dysfunctioning, tubule destruction, fibrosis and specific humoral and cellular responses are claimed to be the underlying reasons [9].

Distal RTA may develop to be primary or secondary. Primary distal RTA may be autosomal recessive or dominant. On the other hand, secondary distal renal tubular acidosis may develop with calcium disorders and genetic and auto-immune disorders. Distal renal tubular acidosis is most frequently accompanied by Sjögren syndrome and lupus erythematosus (SLE) among the auto-immune disorders [8]. In SS, kidney symptoms mainly develop as interstitial nephritis accompanied by hyposthenuria, distal renal tubular acidosis and diabetes insipidus [10]. In cases with kidney involvement, there is a slight decrease in creatinine clearance, and final stage kidney failure is rare. In patients with primary SS with RTA who developed hypopotassemic paralysis, creatinine clearance is lower compared to cases that are not accompanied by paralysis [7,11].

There are only a few case reports stating that primary SS starts as distal renal tubular acidosis (RTA) clinically. Paralysis developed as a result of hypopotassemia due to RTA is a rare symptom in SS, and is seen more frequently in patients with primary SS. If severe hypopotassemia continues for a long time, it causes prevalent loss in muscle force. In this case report, we present a primary SS case developed by clinical distal RTA and presenting with quadruple paralysis due to severe hypopotassemia.

Case Report

A 16-year-old female patient visited to our general internal medicine department due to asthenia, tiredness and nausea. She had been vomiting for the past 2 weeks. The patient had a history of nephrolithiasis, with dryness of mouth and eyes, frequent parotitis attacks and arthralgias since childhood, and the patient had once gone to hospital for amenorrhea. Her family history was unremarkable. Physical examination revealed general state medium, conscious, cooperative and oriented. There were conjunctival hyperemia and dryness of tongue. The patient could only sit with support. Although there was no neurologic deficit presenting ancillary symptoms, the muscle force of the patient was 3/5 in extremes, her deep tendon reflexes were decreased, her plantar reflex was casual, and there was bi-lateral horizontal nystagmus; these were evaluated as quadruple paralysis. The patient's blood pressure was 90/60 mmHg and peak heart rate was 55/min. Other systematic examination results were unremarkable. Immediate examination results are shown in Table 1. In her EKG, sinus bradycardia was (ventricular speed: 52/min.), urine alkaline (Ph: 7) and density was 1005. Routine examination made after immediate treatment are shown in Table 2. In other examinations, creatinine clearance was 60.69 ml/hr; 24-hr urine protein was 148.5 mg/day; urine electrolyte level; K: 52.97 mmol/day (25–125), Na 147.20 mmol/day (40–220), phosphorous: 126 mg/day (400–300). Plasma cortisol level was 19.7 µg/dl (5–25); and free T3, free T4 and thyroid stimulant hormone levels were all within normal values. 25-OH vit D: 7.6 ng/mL (10–50) FANA 1/640 + were found. C3, C4 levels were rather low. Anti ENA SS-A: : >100 IU/ml (n<15), anti ENA SS-B: >100 IU/ml (n<15) values were high. Hepatitis markers were negative. In abdominal US, right kidney had normal localization, normal size, and left kidney had grade 3 pelvic ectasia. It was unremarkable except for an 8 mm radius calculus in the lower pole. In urological consultation, hydronephrosis was deemed to be present due to formerly expelled kidney stones. Schirmer test was made in case of a Sjögren syndrome, 5 mm in the right eye, 8 mm in the left eye was detected and in eye consultation, intensely dry eyes and chronic conjunctivitis were observed; thus, symptomatic treatment was suggested. In examination made due to suspected growth retardation, bone age was congruent with age 14. In the cytogenetic analysis result of the patient with primary amenorrhea, 46 XX karyotype was detected. The values were somatomedin-C: 423ng/ml (226–903 for age 16), LH: 1.91 mIU/ml, FSH: 5.17 mIU/ml, Estradiol: 46.89 pg/ml (6–27); and growth retardation was attributed to the chronic disease. Echocardiography: left ventricular systolic function was normal. Salivary gland biopsy: periductal mononuclear cellular infiltration and focal destruction were detected on 2 areas in minor salivary glands.

As K 1.63 and quadruple paralysis were detected in the immediate examinations of the patient, her first response was made due to hypopotassemic periodic paralysis and parenteral alkaline treatment, and potassium replacement was carried out. There was no change in urinary PH following the ammonium chloride application. Upon taking the results

Table 1. Immediate blood tests.

Plasma	Result	Arterial blood gas	Result
Glucose	89 mg/dl	pH	7.254
Urea	31 mg/dl	PO2	118.9 mmHg
Creatinin	0.6 mg/dl	PCO2	29 mmHg
Na	151 mmol/l	SO2	98.4%
K	1.63 mmol/l	BE	–11.4 mmol/L
Cl	123 mmol/l	cHCO3	14.8 mmol/L
Ca	8.4 mg/dl		
SGOT	38 U/L	Tam idrar	
SGPT	34 U/L	Dansite	1005
LDH	379 U/L	pH	7
CK	202 U/L		

Table 2. Routine tests.

Plasma	Result	Plasma	Result
Total protein	8.9 gr/dl	FT3	3.63 uIU/ml
Albumin	3.76 gr/dl	Parathormone	65.1 pg/mL
Globulin	5.14 gr/dl	Ferritin	53.8 ng/ml
Alkaline phosphatasefe	224 U/L	B12	392.2 pg/ml
GGT	20U/L	Folik asit	6.75 ng/ml
Ca	8.4 mg/dl	WBC	6770 10^3/µL
Fhosphorus	3 mg/dl	RBC	4.39 10^6/µL
Uric acid	3.2 mg/dl	HGB	12.2 gr/dL
Cholestorole	120 mg/dl	HCT	33.3%
Triacylglyceride	64 mg/dl	Platelet	216 10^3/µL
TSH	3.04 uIU/ml	Sedimantasyon	82 mm
FT4	1.23 uIU/ml	CRP	3.1 mg/dL

of medical history record, physical and laboratory examinations, the patient was diagnosed to have primary SS and thus RTA and hypopotassemic periodic paralysis. In nephrology consultation of the patient, it was decided that a biopsy would not be performed, as the patient had hydronephrosis. Parenteral alkaline treatment and potassium replacement were applied, and muscle force returned to normal on the second day of the patient's admission. She was discharged following potassium replacement and 400 mg/day hydroxychloroquine therapy to be monitored by the polyclinic. Check-out laboratory values were Na: 143 mEq/L, K: 3.85 mEq/L, Cl: 109 mEq/L.

Discussion

Sjögren syndrome has a wide clinical spectrum, varying from auto-immune exocrinopathy to systemic disorder; 50% of Sjögren syndrome is primary SS. It is mainly accompanied by dryness of mouth and eyes. The prevalence rate of Sjögren syndrome is about 0.5–5%; female *vs.* male ratio is 9:1. There have been few cases reporting that primary SS developed with distal renal tubular acidosis (RNA) clinically.

This case, where the patient applied with the complaint of quadruple paralysis, is important in that it reveals the results of hypopotassemia due to renal tubular involvement of primary SS. In laboratory examinations made when the patient applied to the emergency polyclinic, the case was diagnosed to be Type I RTA accompanied by normal anion gapped hyperchloremic metabolic acidosis, alkaline urine and hypopotassemia. Potassium and then alkaline replacement was started to be applied to the patient in the clinic, and the symptoms regressed within hours. Following the normalization of the bio-chemical parameters, muscle force returned to normal in 2 days. In light of these data, quadruple paralysis was concluded to have developed in consequence of severe hypopotassemia due to RTA. Starting of primary SS cases as distal RTA clinically is among rare reports in the

literature [11]. Though SS/distal RTA can be seen in all age groups, cases are mostly over age 30 [12]. Considering this, the fact that the symptoms developed at age 16 is another remarkable feature of our case [13].

In the case reported by Poux et al, heart block was detected [14]. Our case did not have heart block, yet there was a sinus bradycardia with 52 beats/min. There was not any other reason detected to explain this sinus bradycardia, except for hypopotassemia. Kidney involvement in SS is mostly due to lymphocytic infiltration of kidney parenchyma. Obvious kidney disorder is seen in approximately 10% of cases with SS, and in 35% of this group there are disorders in urinary acidification. The most frequent disorders observed in this group of cases are hyposthenuria and distal renal tubular acidosis, which were present in our case as well. Proximal renal tubular acidosis as Fanconi syndrome can also be detected, yet less frequently. Eriksson reported that patients with SS that also have Type I RTA have low GFR –a rate of about 44% – and as like this, our case also had a low GFR of 60.69 ml/hr. RTA developed in 73.1% of patients, and 91 were found to have distal RTA [15]. Nine patients presented with hypokalemic paralysis, 4 patients developed Fanconi syndrome, and 3 were proved to have nephrogenic diabetes insipidus. Tubular proteinuria developed in 20.8% of the patients and 13.8% presented glomerular involvement. Renal failure developed in 27.7%. The incidence of chronic interstitial nephritis was 80.5% among all the biopsy materials. Immunofluorescent staining was negative in most renal tissue [16]. Hypergammaglobulinemia was detected in our case, and there was a correlation between distal RTA and hypergammaglobulinemia in case series. Ren et al. suggested renal acidification capacity measurement for patients with hypergammaglobulinemia [16].

Although hypopotassemic paralysis was the symptom that revealed SS, when the medical history was viewed in depth it was seen that xerostomia, arthralgia and parotitis symptoms had also been present before. When other cases in the literature were reviewed, it was observed that prior arthralgia, parotitis, sicca symptoms and symptomatic nephrocalcinosis accompanied quadruple paralysis in some cases [9,11,14]. Immediate initiation of potassium and alkaline replacement and close observation of blood pH and potassium levels are the main principles of the treatment applied to cases that develop with hypopotassemic quadriplegia. It is important to remember that unless the appropriate treatment is applied, hypopotassemic paralysis will also affect the respiratory muscles.

RTA is mostly asymptomatic in primary SS, but it should also be borne in mind that SS may be in the form of hypopotassemic periodic paralysis.

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