Case Report

Severe hypokalaemia and respiratory arrest due to renal tubular acidosis in a patient with Sjögren syndrome

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Key words: hypokalaemia; Sjögren syndrome; renal tubular acidosis; respiratory arrest; tubulo-interstitial nephritis

Introduction

Tubulo-interstitial nephritis and/or renal tubular acidosis occur in almost 25–40% of patients with Sjögren syndrome, characterized by the presence of keratoconjunctivitis, xerostomia and chronic inflammatory sialoadenitis [1,2]. Paralysis of the extremities is well known to be a complication of hypokalaemia due to renal tubular acidosis. A prolonged state of severe hypokalaemia may cause muscle weakness to progress occasionally into respiratory arrest due to paralysis of the respiratory muscle. We present a case of respiratory arrest due to severe hypokalaemia in a patient with Sjögren syndrome.

Case

A 56-year-old woman was transferred to Akita University Hospital by ambulance because of respiratory arrest on February 12, 1998. One month before admission, she consulted a local hospital complaining of general fatigue and weakness of the limbs. She was treated with fluid supplementation after a diagnosis of acute bronchitis and dehydration. However, she developed paralysis of the extremities and dyspnoea. On February 11, she suddenly fell into respiratory arrest. Immediately, she received respiratory assistance with a ventilator and was transferred to the intensive care unit of our hospital. On admission, physical examination revealed mild disturbance of consciousness, severe quadriplegia and very weak voluntary ventilation. Blood pressure was 120/72 mmHg, pulse rate was 84/min with regular sinus rhythm, and body temperature was 36.6°C. There were no abnormal signs observed in the lungs, heart and abdomen. Blood gas analysis revealed that pH was 7.278, PaCO₂ was 33.3 Torr, PaO₂ was 161.9 Torr, HCO₃⁻ was 15.2 mmol/l, base excess was -10.4 mmol/l under oxygen inhalation at 2 l/min. Laboratory data were as follows: serum sodium 149 mEq/l, potassium 1.6 mEq/l, chloride 119 mEq/l, calcium 6.8 mg/dl, phosphate 1.9 mg/dl, creatinine 1.4 mg/dl, blood urea nitrogen 28 mg/dl, uric acid 2.8 mg/dl, blood glucose 162 mg/dl, creatinine kinase 669 U/l, serum amylase 3874 U/l, lipase 18920 U/l, C-reactive protein 0.5 mg/dl, leukocyte count 10 300/mℓ, haemoglobin 8.5 g/dl, platelets 174 000/mℓ. Urinalysis showed urinary pH 6.9, proteinuria 1.3 g/day, haematuria 2+ and β2-microglobulin (β2MG) 80 700 μg/l (normal range 30–250) and N-acetyl-β-D-glucosaminidase (NAG) 24.8 IU/l (normal range 2–12). Urinary potassium excretion was relatively high (44 mEq/day) despite severe hypokalaemia. Based on the above data, we considered that respiratory arrest and quadriplegia were induced by severe hypokalaemia due to renal tubular acidosis (RTA). Continuous intravenous administration of potassium-L-aspartate (about 150 mEq of potassium/day) was started immediately. The next day, respiratory arrest was improved and respiratory assistance was removed as the serum potassium level increased to 2.5 mEq/l. The same therapy was continued till the serum level of potassium normalized. On February 17, the patient was transferred to our department to investigate the cause of RTA.

Laboratory studies in our department revealed that IgG was 3037 mg/dl, IgA was 573 mg/dl, IgM was 150 mg/dl, C3 was 80 mg/dl (normal range 60–119), C4 was 39 mg/dl (normal range 16–43). Anti-nuclear antibody was 1280-fold positive, with a speckled and cytoplasmic pattern. Anti-double-stranded DNA antibody and anti-Sm antibody were negative. Rheumatoid factor was 184 IU/ml. Anti-Ro/SS-A antibody and anti-La/SS-B antibody were positive, 64- and 8-fold, respectively. Thyroid and microsome tests were normal. Thyroid functions were normal. Plasma renin activity was 5.8 ng/ml/h. The serum concentration of
aldosterone was 84 pg/ml. Sialography, with a complaint of xerostomia beginning 1 year earlier, revealed a typical apple tree appearance. Salivary gland biopsy demonstrated severe lymphocytic infiltration and atrophic change of the acinus, compatible with Sjögren syndrome (Figure 1). Renal biopsy, performed on February 26, showed severe lymphocytic infiltration in the interstitium, and tubular atrophy with almost intact glomeruli (Figure 2). We started oral administration of prednisolone (30 mg/day) in addition to potassium citrate after tubulo-interstitial nephritis was diagnosed on March 7. Thereafter, urinary β2MG and NAG were normalized. Prednisolone was tapered gradually.

**Discussion**

Laboratory data, showing severe hypokalaemia (1.6 mEq/l) with metabolic acidosis (pH 7.28) and urinary pH >6.9 suggested the distal type of RTA (dRTA). In this situation, rapid alkalization using sodium bicarbonate alone aggravates hypokalaemia, because serum potassium shifts into the cellular fluid by exchange of H⁺ and K⁺. This patient also had the proximal type of RTA, because of the existence of hypouricaemia, hypophosphataemia, amino aciduria and elevated urinary concentration of β2MG and NAG.

In the differential diagnosis of respiratory arrest, the preceding paralysis of the extremities suggested Guillain–Barré syndrome; however, lumbar puncture showed that this syndrome was not present. Furthermore, immediate improvement of respiratory arrest by potassium supplementation is a further argument against this possibility. There was a slight elevation of serum creatine kinase (CPK 669 U/l). We assume that the respiratory arrest and quadriplegia seen in this patient depended on changes of membrane potential as well as on mild muscle injury associated with hypokalaemia.

The diagnostic criteria of Sjögren syndrome [3] were satisfied by the findings of xerostomia, high titres of anti-Ro(SS-A antibody and anti-La(SS-B antibody, typical apple-tree appearance on sialography and chronic sialoadenitis on salivary gland biopsy. Renal biopsy demonstrated tubulo-interstitial nephritis. We could not detect other causative drugs and diseases that would explain the tubulo-interstitial nephritis except for Sjögren syndrome. The frequency of dRTA in Sjögren syndrome has been reported to be about 25–40% [1,2]. There are many case reports of Sjögren syndrome associated with hypokalaemic quadriplegia [4–10]. Tsuboi et al. described that periodic paralysis was observed in almost 40% of Sjögren syndrome cases associated with dRTA [10]. However, only three cases were reported that respiratory arrest depends on severe hypokalaemia associated with renal tubular acidosis due to various causes (Table 1) [11–13]. Bridi et al. and Koul and Saleen presented cases of females having RTA associated with chronic active hepatitis [11,12]. Also there is only one case report describing respiratory failure due to Sjögren syndrome [13]. The potassium level in these cases was 0.8 mEq/l [11], 1.7 mEq/l [12], 1.4 mEq/l [13] and 1.6 mEq/l in our case. There is no significant difference at the level of serum potassium between the respiratory arrest group and quadriplegia alone group (1.0–2.8 mEq/l). These results suggest that the progress for respiratory arrest may be influenced by interindividual differences in sensitivity toward hypokalaemia (and presumably also transmembrane K gradient) of respiratory muscle. Even patients with hypokalaemia <1.7 mEq/l were liable to develop respiratory arrest. The above four cases, including our own, were all female, and showed good prognosis with immediate respiratory support and potassium supplementation. However, Nimmannit et al. [14] described fatal cases of hypokalaemic respiratory failure and ventricular fibrillation due to endemic RTA in Thailand. This condition occurred in otherwise healthy young males and sometimes resulted in nocturnal death which is different from the present case.

In primary Sjögren syndrome, RTA commonly is asymptomatic. However, if such a state persists, patients will develop quadriplegia. Furthermore, if adequate treatment is not received, muscle paralysis...
Table 1. Case reports of respiratory arrest associated with RTA

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Minimum K</th>
<th>Origin of RTA</th>
<th>Renal biopsy</th>
<th>Prognosis</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>18</td>
<td>0.8 mEq/l</td>
<td>CAH</td>
<td>TIN, MN</td>
<td>improved</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>8</td>
<td>1.7 mEq/l</td>
<td>CAH</td>
<td>ND</td>
<td>improved</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>38</td>
<td>1.4 mEq/l</td>
<td>SjS</td>
<td>TIN</td>
<td>improved</td>
<td>13</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>56</td>
<td>1.6 mEq/l</td>
<td>SjS</td>
<td>TIN</td>
<td>improved</td>
<td>this study</td>
</tr>
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CAH, chronic active hepatitis; SjS, Sjögren syndrome; TIN, tubulo-interstitial nephritis; MN, membranous nephropathy; ND, not done.

may progress to respiratory arrest. Although respiratory arrest associated with Sjögren syndrome is very rare, this complication is very severe and can be fatal. It is important to pay attention to the occurrence of severe hypokalaemia with metabolic acidosis and provide adequate treatment for this combination in patients with Sjögren syndrome.

References


Received for publication: 6.4.99
Accepted: 20.4.99