Hypokalaemia paralysis as the presenting manifestation of primary Sjögren’s syndrome


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Key words: hypokalaemia; renal tubular acidosis; serum anion gap; Sjögren’s syndrome; Urine anion gap

Introduction

Although hypokalaemia in patients with Sjögren’s syndrome is a frequent sequela of renal tubular acidosis (RTA), severe symptomatic decrease in serum potassium concentration has been described only in few cases [1-8]. We report a case with hypokalaemic paralysis as the presenting finding of primary Sjögren’s syndrome.

Case Report

A 27-year-old woman was admitted to our hospital with a 3-day history of progressive weakness. For the previous 2 weeks the patient had complained of nausea and reported episodes of vomiting with decrease in food and water intake. The patient denied use of drugs affecting acid–base and electrolyte parameters like herbal medicines. On examination, flaccid paralysis of the four limbs was found. Blood pressure was 130/70 mmHg, heart rate 94/min, temperature 36.9°C, and respirations 16/min. The rest of the physical examination was unremarkable. Laboratory investigation at the time of admission is shown in Table 1.

The patient recovered gradually within 2 days with potassium replacement.

According to the laboratory findings the diagnosis of hyperchloremic metabolic acidosis with a normal serum anion gap was evident. Moreover, severe hypokalaemia with kaliuresis (urine potassium 26 mmol/l, FE K+ 8%, TTKG 12), increased urine pH and hypovolaemia (increased ratio of urea/creatinine and low urine sodium) were also present. Urine anion gap was positive (12 mmol/l) despite the high urine Cl– concentration. Correction of the hypovolaemia and hypokalaemia with the use of NaCl 0.9% and KCl 10% solutions did not correct either the metabolic acidosis or the alkaline urine pH (arterial pH reached 7.32, and urine pH reduced to 7). The existence of hyperchloremic metabolic acidosis, which remained stable after the correction of the coexistent hypovolaemia and hypokalaemia, with alkaline urine pH in the absence of infection with a urea-splitting organism and with increased urine anion gap was indicative of RTA.

Laboratory investigation for the presence of proximal tubular dysfunction was negative (Table 2). Although our patient had no evidence of Sjögren’s

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Table 2. Investigation of proximal tubular function

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>serum PO₄ (mmol/l)</td>
<td>0.97</td>
</tr>
<tr>
<td>FEPO₄⁻ (%)</td>
<td>17</td>
</tr>
<tr>
<td><strong>Tm PO₄²⁻ / GFR</strong></td>
<td>2.8</td>
</tr>
<tr>
<td>serum uric acid (mmol/l)</td>
<td>208</td>
</tr>
<tr>
<td>24-h urine uric acid (mmol)</td>
<td>23.8</td>
</tr>
<tr>
<td>Urine uric acid/creatinine</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

No glucosuria or aminoaciduria were present

\[
*\text{FEPO}_4^-\text{ (%) } = \frac{\text{Urine PO}_4^-\times \text{serum creatinine}}{0.95 \times \text{serum PO}_4^- \times \text{urine creatinine}} \times 100
\]

A FEPO₄⁻ more than 20% is considered as inappropriate phosphaturia.

**Tm PO₄⁻ / GFR** was calculated from a nomogram using plasma PO₄⁻ concentration and % TRP (percentage tubular reabsorption of phosphate) (Normal values 2.5 - 3.5).

Discussion

RTA is a frequent extraglandular manifestation of primary Sjögren's syndrome with an incidence of about 30% [9,10]. Hypokalaemia commonly accompanies the disease, especially its complete type [10]. However, severe symptomatic hypokalaemia is rare [1-8]. Hypokalaemia in renal tubular acidosis is correlated with reduced distal H⁺ secretion. As a result, Na⁺ reabsorption must occur in exchange for K⁺ if Na⁺ balance is to be maintained. In addition to these factors, distal flow may be directly increased in metabolic acidosis because of decreased passive reabsorption in the proximal tubule. One-third of proximal Na⁺ reabsorption is passive, occurring downhill of created primarily by HCO₃⁻ reabsorption. In metabolic acidosis less HCO₃⁻ is reabsorbed proximally (since less is filtered), thereby decreasing passive NaCl and water transport and augmenting distal delivery [11]. Moreover, the presence of alkaline urine in our patient might have enhanced potassium excretion [12]. In our case both kaliuresis (due to above mechanisms) and decreased potassium intake (due to nausea) could have contributed to the severe hypokalaemia.

The presence of type 1 RTA should be suspected in any patient with hyperchloraemic metabolic acidosis and a urine pH greater than 5.3. In the absence of a high urine pH due to infection with an urea-splitting organism, the only other conditions that can produce this combination are type 2 RTA, volume depletion [13,14] and hypokalaemia [15]. Although hypokalaemia and volume depletion were evident in our patient at the time of admission, the appropriate correction of these abnormalities did not correct metabolic acidosis or cause a decrease of urine pH. The absence of proximal tubular dysfunction presumably rules out the existence of RTA type 2, although a bicarbonate loading test was not performed. Urine anion gap is a useful index of NH₄⁺ excretion and in conjunction with the serum K⁺ and urine pH can help in the diagnosis of RTA [13]. A positive urine anion gap is indicative of a decreased NH₄⁺ excretion and RTA.

As in some previously reported cases hypokalaemia led to the diagnosis of RTA and Sjögren's syndrome. However, in most of the reported cases some glandular manifestations of Sjögren's syndrome were present. The interesting finding in our case is that no symptoms or signs were present to suggest Sjögren's syndrome. In addition, both Schirmer and rose bengal tests gave normal results. Labial biopsy revealed focal lymphocytic infiltration greater than 2 + according to Tarpley classification. In view of these findings percutaneous kidney biopsy was performed, when serum potassium was 3.4 mmol/l (with the use of potassium citrate orally). Kidney biopsy revealed areas of interstitial infiltration with lymphocytes and plasmacytes with normal glomeruli.

Immunological investigation revealed polyclonal hyperglobulinaemia without monoclonal paraproteins on high-resolution gel electrophoresis, RF 1/80, ANA 1/1280, speckled pattern, C₃ 0.82 g/l (normal values 0.53-1.25 g/l), C₄ 0.36 g/l (normal values 0.2-0.49 g/l), anti-ds DNA negative and anti-Ro (SSA) positive. However, both Schirmer and rose bengal tests gave normal results. Labial biopsy revealed areas of interstitial infiltration with lymphocytes and plasmacytes with normal glomeruli.

Syndrome, the presence of an unexplained renal tubular acidosis as well as the elevated serum total protein concentration led us to look for the presence of subclinical Sjögren's syndrome.

Hypokalaemia and hyperchloraemia in RTA are associated with the demonstration of interstitial inflammatory process. Various studies have suggested that lymphocytic and plasma cell infiltrates surrounding renal tubules are associated with and may cause a renal tubular defect. However, like Shioji et al. [5] we also noted that RTA was not always associated with the demonstration of interstitial infiltrate in renal biopsies [9]. Thus it seems unlikely that interstitial nephritis is the sole cause for the development of RTA in primary Sjögren's syndrome [10]. Although hyperglobulinaemia and cryoglobulinaemia have been regarded as the pathogenetic mechanisms of RTA, it seems that they are not the major causes for the development of RTA in primary Sjögren's syndrome [9,10].

The demonstration and identification of monoclonal proteins in the blood and the urine of patients with primary Sjögren's syndrome was previously reported. The possibility of a 'toxic' effect of these monoclonal proteins to the renal tubules could be an important pathogenetic mechanism for the development of RTA [10].

Finally, in some patients with RTA the distal urinary acidification defect could be due to the absence of H⁺-ATPase in the intercalated cells. This immune-mediated suppressed expression of the H⁺-ATPase in the kidney...
is the suggested mechanism for type 1 RTA observed in a patient with Sjögren's syndrome [16].

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References


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