Hypokalemic Paralysis: A Hidden Card of Several Autoimmune Diseases

Yelitza Velarde-Mejía1, Rocio Gamboa-Cárdenas1, Manuel Ugarte-Gil1,2 and César Pastor Asurza1,3

1Rheumatology Department, Hospital Guillermo Almenara Irigoyen, La Victoria, Peru.
2School of Medicine, Universidad Científica del Sur, Villa El Salvador, Peru. 3School of Medicine, Universidad Nacional Mayor de San Marcos, Lima, Peru.

ABSTRACT: Acute hypokalemic paralysis is a rare and potentially fatal condition, with few related causes, one of which highlights distal renal tubular acidosis (dRTA). Distal renal tubular acidosis is a rare complication of several autoimmune diseases such as systemic lupus erythematosus, Sjögren’s syndrome, and Hashimoto thyroiditis. We report a case of a lupic patient who presented rapidly progressive quadriparesis in the context of active renal disease. Research revealed severe refractory hypokalemia, metabolic acidosis, and alkaline urine suggestive of dRTA. We diagnosed Sjögren’s syndrome based on sicca symptoms, an abnormal salivary glands’ nuclear scan and the presence of anti-Ro/SSA and anti-La/SSB. In addition, the finding of thyroid peroxidase, thyroglobulin antibodies, and hypothyroidism led us to the diagnosis of Hashimoto thyroiditis. Due to the active renal involvement on the context of systemic lupus erythematosus and Sjögren’s syndrome, the patient received immunosuppression with rituximab, resulting in a progressive and complete improvement.

KEYWORDS: lupus erythematosus, systemic, renal tubular acidosis, hypokalemias

RECEIVED: March 8, 2017. ACCEPTED: June 19, 2017.

PEER REVIEW: Four peer reviewers contributed to the peer review report. Reviewers’ reports totaled 442 words, excluding any confidential comments to the academic editor.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: Yelitza Velarde-Mejía, Rheumatology Department, Hospital Guillermo Almenara Irigoyen, Av. Grau s/n, La Victoria LIMA 13-15033, Peru. Email: ginger12887@hotmail.com

Introduction

Acute hypokalemic paralysis (AHP) is a potentially fatal but reversible condition which constitutes a challenge for emergency physicians. Secondary AHP is related to few conditions and its ultimate course can be avoided with a rapid correction of hypokalemia. A proper clinical evaluation aimed at determining its underlying cause should always take place. One of its main causes, but many times overseen, is distal renal tubular acidosis (dRTA), which is a disorder characterized by an abnormal tubular acidification, resulting in hypokalemia and hyperchloremic metabolic acidosis with a normal serum anion gap (AG). Not frequently, dRTA could lead to AHP. Autoimmune disorders such as systemic lupus erythematosus (SLE), Sjögren’s syndrome (SS), and Hashimoto thyroiditis (HT) may cause secondary dRTA and should always be excluded. We report the case of a patient with AHP secondary to dRTA, with more than one autoimmune disorder commonly associated with this condition, who had a good response to immunosuppression with rituximab (RTX).

Case Presentation

A 45-year-old woman was admitted to the emergency service with a 3-hour condition of tachypnea and flaccid quadriparesis. She had a 7-year history of SLE (her initial symptoms were malar rash, photosensitivity, nonerosive polyarthritis, and positive antinuclear antibodies with homogeneous pattern, titer 1/2560) whose main involvement was a proliferative glomerulonephritis and a recent diagnosis of hypothyroidism. Systemic lupus erythematosus was treated with prednisone (PDN) at varying doses and hydroxychloroquine and mycophenolate mofetil (MMF) with doses between 1.5 and 3 g/d (current dosage) with complete renal response. Before 10 months of this episode, she presented a proteinuric flare (24-hour urine protein test: 760 mg/dL) poorly followed due to the lack of patient’s compliance. Before 3 weeks of admission, she began complaining of mild myalgias and cramps which she attributed to her job. On admission, the patient denied vomiting, diarrhea, and the use of other drugs besides her usual medications. Her biologic functions were normal. She was tachycardic, with a normal blood pressure. Arterial blood gases demonstrated metabolic acidosis with normal serum AG, hypoxemia, and severe hypokalemia (K: 1.4 mEq/L) with electrocardiogram changes (presence of U wave and flattening of the T wave). Laboratory tests showed serum potassium at 1.7 mEq/L, high titer of anti–double-stranded DNA, and low complement. Cortisol, glucose, creatinine, calcium, magnesium, and liver profile were normal, and creatine kinase was mildly elevated (246 U/L). Urinalyses showed telescoped urinary sediment—an alkaline urinary pH (7.8). A renal ultrasonography revealed bilateral chronic nephropathy.

She received 2 intravenous replacement doses of potassium (5.4 mEq), but serum potassium remained low (1.7 mEq/L). She was admitted to the Rheumatology Department tachypneic with flaccid quadriparesis. Despite intense potassium replacement therapy, serum potassium remained in the hypokalemic range (<2.5 mEq/L) with persistent respiratory distress. Therefore, other possible causes of respiratory distress...
such as pulmonary thromboembolism (normal lung scintigraphy), pulmonary hypertension, and pericardial effusion (determined by echocardiography) were ruled out. Clinical improvement was evident (normal respiratory rate and pattern and the ability to stand, walk, and sit up in bed unassisted) a few hours after a continuous potassium infusion pump was placed. Potassium replacement was continued with an oral solution of citric acid (Shohl's modified solution). In addition, the diagnosis of dRTA was confirmed on the basis of an acid-base disorder in most of the patients with a secondary cause, plus the age of presentation usually associated with iatrogenic thyrotoxicosis, was also excluded because our patient had not modified her levothyroxine doses, and her thyroid-stimulating hormone (TSH) and triiodothyronine (T3) were normal (TSH: 0.82 mUI/L; T3: 4.0 pg/mL).

The diagnosis of dRTA was established on the basis of hyperchloremic metabolic acidosis with normal AG, alkaline urine, positive urinary AG (urine Na+ of 265 mEq/L, K+ of 38 mEq/L, and Cl− of 240 mEq/L) and severe, refractory hypokalemia. In this disorder, the abnormal metabolic profile is a result of an excessive renal loss of potassium due to impaired secretion of H+ in the distal nephrons. It has distinctive features and could have a primary or secondary cause (Table 2).5-7 Acquired dRTA is often secondary to autoimmune diseases6,8 (SLE, SS, and HT, among them).

In HT, only a few cases of RTA have been reported. In murine models, thyroid hormones have been related to an abnormal expression of acid-base transporters, with increased membrane cell Na+/K+-ATPase pumps and reduced elimination of H+ ions in the distal nephron. The existence of antibodies against the collector tubules has been suggested as possible cause6 supporting the occasional need for corticosteroid treatment in these patients.11 The prevalence of dRTA in SLE has not been asserted properly because of the few reported cases. Of note, concurrent active proliferative glomerulonephritis and RTA have been described.12,13 The precise mechanisms of tubular damage in SLE have not been elucidated yet; however, the deposition of immunoglobulins, complement, and plasma cells around tubules which may lead to irreversible damage suggests that the ongoing SLE autoimmune process is involved in its pathogenesis.14

In contrast to HT and SLE, tubulointerstitial renal involvement is a relative common manifestation of SS with an estimated prevalence of 5% to 10%.15-20 The pathogenesis of dRTA in SS is not completely understood, but some studies suggest that the absence of H+-ATPase pump and the presence of autoantibodies to intercalated cells in the collector duct and against carbonic anhydrase in the distal nephron are the

**Table 1. Common causes of hypokalemic paralysis.**

| Classification | Hypokalemia Paralysis |
|----------------|------------------------|
| a. Periodic paralysis due to intracellular shift | Thyrotoxic periodic paralysis |
| Hypernatremic hypokalemia paralysis | |
| b. Patients with hypokalemia paralysis due to potassium deficit | Excessive vomiting |
| Diuretics | Bartter or Gitelman syndrome |
| Primary aldosteronism | |
| With hypochloremic metabolic alkalosis | Distal renal tubular acidosis |
| Acute severe diarrhea | |

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In conclusion, hypokalemia could be an inadvertent cause of flaccid paralysis and might even lead to death. Besides, refractory hypokalemia associated with metabolic acidosis should suggest the diagnosis of dRTA and lead to the search of secondary causes, being the autoimmune diseases (SLE, SS, and less frequently HT) the most important among them. Finally, potassium replacement and immunosuppressive treatment should be individually adjusted to each patient; long-term follow-up should monitor muscle strength, serum electrolytes, and renal function.

Acknowledgements
The authors thank Graciela S Alarcón, MD, MPH, MACR, for providing expert assistance in the review of this manuscript.

Author Contributions
All authors were responsible for case conception, critical revision and drafting of the manuscript. All authors approved the final version to be published.

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Table 2. Conditions associated with distal RTA.

| PRIMARY                          | SECONDARY                        |
|----------------------------------|----------------------------------|
| Autosomal-dominant RTA           | Sjögren’s syndrome               |
| Autosomal-recessive RTA          | Systemic lupus erythematous      |
| Pseudohypoaldosteronism type II  | Chronic active hepatitis         |
|                                  | Hashimoto thyroiditis            |
|                                  | Takayasu arteritis               |
|                                  | Myeloma                          |

Abbreviation: RTA, renal tubular acidosis.
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