Ibuprofen Abuse—A Case of Rhabdomyolysis, Hypokalemia, and Hypophosphatemia With Drug-Induced Mixed Renal Tubular Acidosis

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INTRODUCTION

Drug-induced renal tubular acidosis (RTA) can pose an uncommon but important cause of severe potassium wasting and hypokalemia. We report a case of distal RTA causing severe hypokalemia and rhabdomyolysis in a patient who consumed large amounts of ibuprofen.

CASE PRESENTATION

A 48-year old, previously healthy African American woman was admitted to the Medical intensive care unit with complaints of diffuse myalgias and severe generalized weakness of all extremities and polyuria for a few weeks. She had suffered a distal tibio-fibular stress fracture 5 months before, which was complicated by delayed union. Her admission laboratory values revealed severe hypokalemia, a non-anion gap metabolic acidosis with a positive urine anion gap, and a urine pH of 6.5, consistent with distal (type 1) RTA (Table 1). She also had spontaneous, nontraumatic rhabdomyolysis secondary to severe hypokalemia, but with hypophosphatemia resembling proximal RTA (type 2). She was also noted to have low 25-OH vitamin D, mild transaminitis, and *Escherichia coli* cystitis. She had urinary wasting of potassium of 104 mmol/24 h (normal is <30 mmol). Upon further questioning, the patient revealed that she had been taking about 20 tablets of ibuprofen tablets daily (~4 g/d) for the last 3 months to control her ankle pain. She tested negative for Sjögren's disease, other autoimmune disorders, and paraproteinemia. With continued aggressive fluid and electrolyte replacement, vitamin D therapy, and cessation of all nonsteroidal anti-inflammatory drugs, her biochemistries normalized and she was discharged in 5 days. She was followed up in clinic in a week, at which time repeat serum chemistries were noted to be normal.

DISCUSSION

Our patient developed severe hypokalemia and distal RTA most likely due to ibuprofen use. Atypical

Table 1. Laboratory values

Serum chemistry (reference)	Comments
VBG: **7.27/45/40/20** on room air	Mixed non-anion gap metabolic acidosis, anion gap metabolic acidosis, and respiratory acidosis
Na: 141 (135-145 mmol/l)	
K: **1.2** (3.5-5.1 mmol/l)	
Cl: 111 (98-107 mmol/l)	Anion gap may be related to lactic acidosis and unmeasured organic anions released from damaged muscle. Alcohols and ketones were not detected in blood in this case
CO_2: **16** (22-32 mmol/l)	
BUN: 10 (6-20 mg/dl)	
Cr.: 0.8 (0.4-1.0 mg/dl)	
Albumin: 3.9 (3.5-5.0 g/dl)	
CK: **28880** (38-234 IU/l)	
Myoglobin: 8514 (3–70 ng/ml)	
Vitamin D: **<4.0** (30–100 ng/ml)	
PTH **194** (12–88 pg/ml)	
P: **1.2** (2.5–4.5 mg/dl)	
Ca: 8.9 (8.6–10.2 mg/dl)	Respiratory acidosis may be related to hypoventilation secondary to respiratory muscle weakness in severe rhabdomyolysis Vitamin D deficiency and secondary hyperparathyroidism
Urine chemistry	
Urine pH **6.5**, glucose: **negative**; protein: **100** mg/dl, WBC 26–50/hpf, RBC 3–5/hpf, few hyaline casts	
Na[a]: 69 mmol/l	UAG: 8.1 (Positive UAG)
K[a]: 20.5 mmol/l	Ur. K/Ur. Cr ratio 43 mEq/g (>13 is considered significant renal loss) 24-h K secretion of >30 mmol is considered significant
Cl[a]: 78 mmol/l	
Cr[a]: 22 mg/dl	
PO_4[a]: 14 mg/dl	
Osm: 263 mmol/l	Polyuria may be related to impaired concentration ability of tubules in the presence of hypokalemia
24-h K: 104 mmol/24 h	
24-h Urine volume: 7.3 L	

BUN, blood urea nitrogen; CK, creatine kinase; hpf, high-power field; PTH, parathyroid hormone; RBC, red blood cell; UAG, urine anion gap; VBG, venous blood gas; WBC, white blood cell.
Bold data are abnormal laboratory values.
[a]Spot urine measurements.

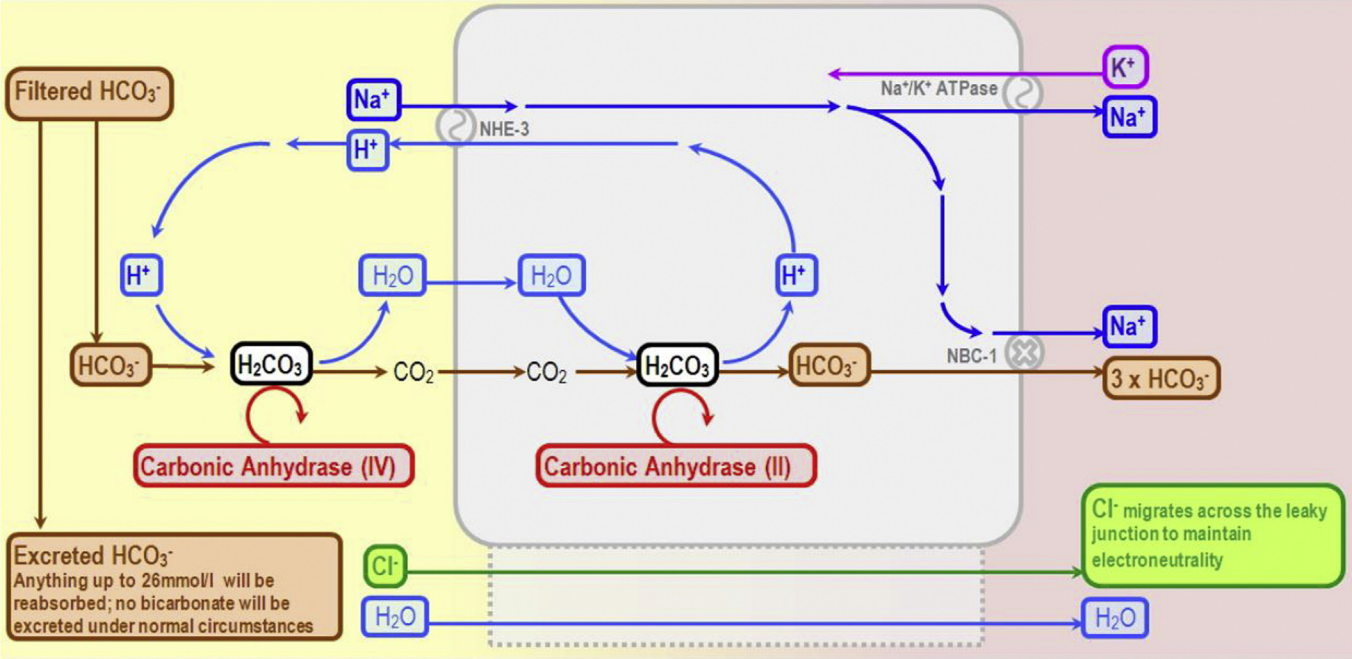

Figure 1. Bicarbonate handling in the proximal tubule. Reprinted from Yartsev A. Acid-base disturbances. Core topics in intensive care. In: *Deranged Physiology*. Chapter 5.1.1. Available at: https://derangedphysiology.com/main/core-topics-intensive-care/acid-base-disturbances/Chapter%205.1.1/type-2-renal-tubular-acidosis-and-acetazolamide. Accessed July 2018.

features here are hypophosphatemia and urinary phosphate wasting; however, these may be due to the patient's underlying vitamin D deficiency. Only a few cases have been reported of ibuprofen causing either proximal- or distal-type RTA.[1–3] This is thought to be related to its inhibitory effect on carbonic anhydrase II as mentioned in Figure 1.[4,5]

CONCLUSION

This case highlights the potential of ibuprofen to cause a type 3 RTA–like picture, or a mixed type 1 and 2 RTA with life-threatening hypokalemia to the extent of causing rhabdomyolysis.

DISCLOSURE

All the authors declared no competing interests.

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