

REFRACTORY HYPOKALEMIA: A CASE OF TOPIRAMATE-INDUCED RENAL TUBULAR ACIDOSIS (RTA)

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CASE PRESENTATION: A 50-year-old woman presented with hypokalemia (2.7 mmol/L) 11 months after initiating topiramate for migraine headaches. She was also receiving lisinopril/hydrochlorothiazide (HCTZ). She remained hypokalemic despite stopping lisinopril/HCTZ and potassium chloride (KCl) 100 mEq/day. Hyperaldosteronism was not present. The urinary K excretion was 133 mmol/day (normal 30-90). The arterial blood gas was: pH 7.38, PCO₂ 33.5 mmHg and bicarbonate (HCO₃⁻) 19 mmol/L. The urine anion gap was 23. Two tiny stones were present in the right kidney. After decreasing topiramate to 200 mg/day, severe ocular migraines developed. She resumed topiramate 300 mg/day and KCl 100 mEq/day. Subsequent 24 hr urinary chemistries one year later were: pH 6.0, citrate 75 mg (normal ≥ 370), K 158 mmol and calcium 331 mg (normal 20-275). The serum Cl was elevated at 111 mmol/L and the serum HCO₃⁻ was low at 20 mmol/L. She had elevated supersaturation indices for brushite and hydroxyapatite crystals. KCl was changed to K citrate 100 mEq/day. Divalproex was later substituted for topiramate, and K citrate was tapered and discontinued. The serum K, Cl and HCO₃⁻ normalized on KCl 40 mEq/day. The 24 hr urinary K was 98 mmol/day and the urinary pH was 6.0. KCl was stopped and her serum K, Cl, and HCO₃⁻ remained normal. Her stones remained inactive. Her migraine headaches remained controlled with divalproex.

CONCLUSION: This case illustrates the importance of considering drug-induced renal tubular acidosis (RTA) in the etiology of refractory hypokalemia and nephrolithiasis. Topiramate may induce both a proximal (type 2) and distal (type 1) RTA (i.e., mixed [type 3] RTA) by inhibiting the activity of cytosolic type II carbonic anhydrase in a manner similar to acetazolamide. Both severe metabolic acidosis and refractory hypokalemia have been reported with topiramate. There is no apparent correlation with topiramate dose, and metabolic abnormalities typically resolve after stopping the medication. Monitoring serum K and HCO₃⁻, as well as advising increased fluid intake to prevent nephrolithiasis, is warranted after initiation of topiramate.