CKD and Occult Type I RTA Manifesting as Cryptic Paroxysmal Weakness and Hypokalemia

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INTRODUCTION

Hypokalemia is a commonly encountered electrolyte abnormality, prompting frequent hospital admissions. The etiology is often iatrogenic or via gastrointestinal losses, however in otherwise healthy adults the differential should be broadened. When combined with non-gap metabolic acidosis, a Rental Tubular Acidosis should be entertained.

CASE DESCRIPTION

A 31-year-old recently immigrated Filipino woman with reported history of long standing episodic hypokalemia, paroxysmal polyuria and severe generalized muscular weakness, with a family history of early renal failure, was hospitalized following 2 days severe progressive weakness, fatigue, polyuria and hand cramping in the setting of recent physical exertion. She was diagnosed with Periodic Paralysis (PP), but despite over-the-counter potassium supplements, which she had taken sporadically for 12 years following an ICU admission for the same in the Philippines, her symptoms noted above periodically recurred. Records from Philippines not available.

Family history: notable for middle age onset ESRD (father)

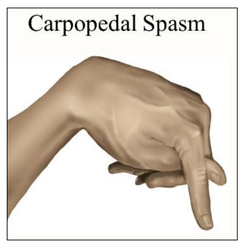
Exam: notable for short stature, bilateral carpopedal spasms, and initially asymmetric 4-/5 motor weakness

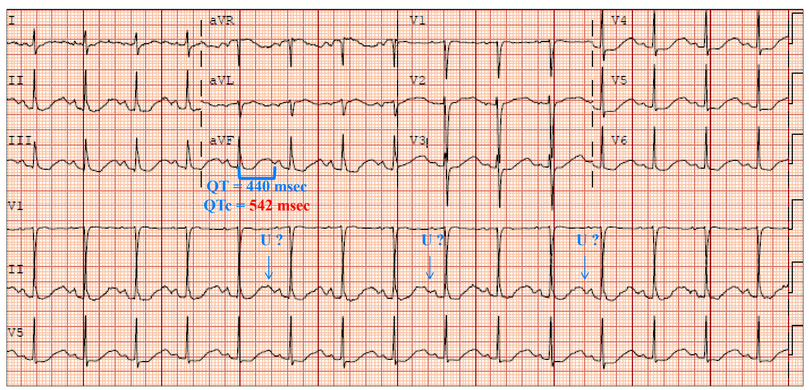
Studies: (below and ECG)

Imaging: Bilateral renal U/S: highly echogenic, c/w → chronic renal disease.

Urine	Serum	Serum
pH 7.0	Potassium 2.0	Creatinine 1.54
Sodium: 39	Bicarbonate 16	eGFR 38
Potassium: 10	Anion Gap 11	pH 7.31
Chloride 44	Phos 1.4	Calcium 7.5
(-) Casts	Chloride 110	(-) SPEP, UPEP
(-) Ca^{2+}crystal	+ Protein Gap	Neg HIV, HCV

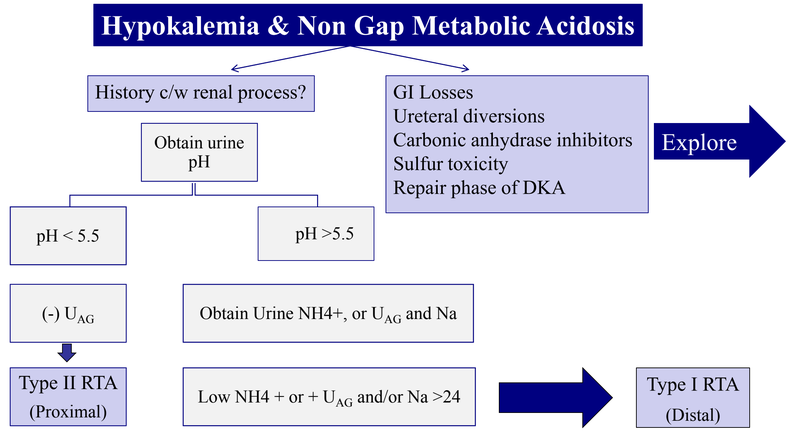
Carpopedal Spasm





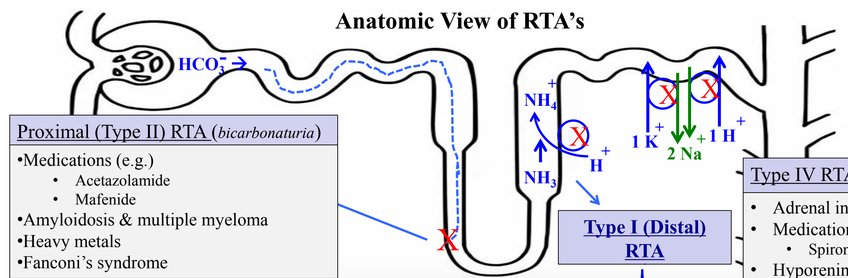
DIFFERENTIAL DIAGNOSIS

This woman carried diagnosis of periodic paralysis (PP) described as episodic hypokalemia and weakness, however her presentation was not consistent, since acidosis is not a feature and potassium usually reverts to normal after repletion or succession of exercise. Due to hypokalemia and non gap metabolic acidosis, without evidence of excessive GI loss or other causes, work up for RTA ensued.



It is prudent to identify underlying etiology of distal RTA (Figure below), as it can lead to nephrocalcinosis and/or osteoporosis, medication toxicity, or various primary kidney tubular defects. In our case, autoimmune workup, nephrocalcinosis and medication toxicity was ruled out. Given her father's cryptogenic, early-onset ESRD, her short stature (far below expected mid-parental height), unexplained CKD, recurrent (vs persistent) weakness and potassium disorder, she was diagnosed with a probable familial distal type I RTA. Although her Urine AG was negative this can be explained by her volume depletion secondary to her polyuria at time of admission/urine studies.

Anatomic View of RTA's



Proximal (Type II) RTA (*bicarbonaturia*)
- Medications (e.g.)
  - Acetazolamide
  - Mafenide
- Amyloidosis & multiple myeloma
- Heavy metals
- Fanconi's syndrome

Type I (Distal) RTA

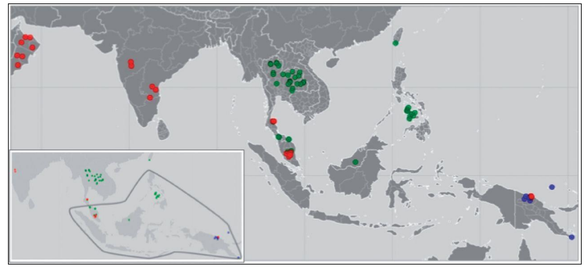
Type IV RTA (↓*Aldo effect*)
- Adrenal insufficiency
- Medications (e.g.)
  - Spironolactone, etc
- Hyporenin/hypoaldo
  - Diabetes
  - Hypertension
    - Nephrosclerosis
  - Chronic Interstit. Neph
- Mineralocorticoid resist.

Primary	Secondary	Medication	Hypercalciuria	Other
• Idiopathic • Familial • AD & AR • Distal tubule intercalated cells	• Sjögren synd. • Autoimm hepat. • PBC, SLE, RA	• Ifosfamide • Ampho. B • Lithium • Ibuprofen	• hyperPTH, • Vitamin D intoxication	• Obstructive urop. • Transplant rejection • Wilson disease • Medullary sponge kidney

DISCUSSION

In a clinical profile, a cause of distal RTA can be established in 54% of patients, primarily due to an autoimmune or urologic defect. Distal RTA is a heterogeneous pathology, resulting in a wide presentation across a clinical spectrum pending age of presentation, underlying primary etiology, and baseline renal function. Proximal muscle weakness and hypokalemic paralysis were the dominant presentations[1]. Other clinical manifestations include polyuria, polydipsia, failure to thrive, bony deformities, short stature (especially in hereditary/congenital cases), and not uncommonly nephrolithiasis and nephrocalcinosis.

A World View of "tropical" Genetic dRTA[1]



The above highlights patterns of geographical autosomal recessive mutations of SLC4A1 gene, which makes proteins on distal collecting duct and is notable for a high prevalence in Thailand, Malaysia, Philippines, and Papua New Guinea[1].

In our patient, secondary causes were essentially ruled out. In light of her father's early history of ESRD, her renal insufficiency, short stature, and recurrent electrolyte derangements, it is highly plausible to assume she has a genetic dRTA.

Management

1. Evaluate for nephrolithiasis and nephrocalcinosis with renal U/S
2. Alkalize urine with Na^+ biocarbonate in attempt to correct metabolic acidosis
3. Amiloride to reduce K+ excretion, in addition to K+ supplements
4. Evaluate for underlying causes: Autoimmune work up: RF, ANA, anti-CCP, Sjögren's Ab , family history

Conclusion

1. The incidence of RTA is underestimated
2. Be suspicious when patients present with multiple or unexplained mild or severe metabolic derangements
3. Distal RTA, etiology can be congenital, familial, iatrogenic, but also a first manifestation of a secondary pathology (AI)
4. Early diagnosis may improve bones, target height and prevent CKD

Reference

1. Khositseth, S, et al. Tropical distal renal tubular acidosis: Clinical and epidemiological studies in 78 patients. *Qjm, 105*(9), 861-877. 2012. doi:10.1093/qjmed/hcs139