A PH PARADOX: RENAL TUBULAR ACIDOSIS IN PREGNANCY

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Objectives

- Review causes and management of Renal Tubular Acidosis in Critical Care Medicine
- Recognize that pregnancy is a physiologic state which can precipitate and exacerbate RTA
- Recognize the fetal complications of untreated metabolic acidosis from RTA

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Any names or ages used on the upcoming slides are fictitious and not referring to an actual patient.

Introduction

- Renal Tubular Acidosis is a normal anion gap metabolic acidosis resulting from either defective kidney excretion of acid or reabsorption of bicarbonate
- 3 major forms:
  - *Type 1 (distal RTA): distal tubular acid secretion is impaired, associated with hypokalemia*
  - *Type 2 (proximal RTA): renal bicarbonate reabsorption in proximal tubule is impaired, associated with hypokalemia*
    - Associated with Fanconi syndrome
  - *Type 4 (hyperkalemic distal RTA): distal tubule impaired electrolyte transport including sodium, chloride, and potassium*
    - Associated with hypoaldosteronism or inadequate renal response to aldosterone

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Case Presentation

- 39 year old Female G4P3 at 32 weeks gestation with past history of peripartum cardiomyopathy, gestational diabetes, and maternal sepsis secondary to Lyme disease, transferred from outside hospital for fevers, SVT, and shock
- Outside Hospital Course:
  - *Attempts to control SVT including AV nodal blocking agents, Cardioversion x 2, and finally high dose adenosine with transient termination of tachycardia*
- In Transit, patient became hypotensive with worsening tachycardia and was started on vancomycin and piperacillin/tazobactam with 500 cc fluid bolus for concerns of septic shock

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On Presentation:

- Endorsed progressively worsening dyspnea and numbness in legs and arms for several days
- Denies any cough, sputum production, dysuria, fevers prior to presentation, or GI symptoms
- Vital Signs: 96/46 (62), HR 122, SpO2 99% on 4L NC, RR 25, Afebrile
- Exam: Fatigued, regular tachycardia, increased respiratory effort, lungs clear to auscultation, gravid abdomen without tenderness to palpation, 5/5 strength in upper and lower extremities, sensation intact
- Labs:
  - *pH 7.35, PaCO2 20.3 mmHg, Serum Bicarb 11 mmol/L*
  - *Potassium 2.9*
  - *Chloride 115*
  - *BUN 6, Cr 0.8*
  - *AG 12*
  - *Calcium 6.8*
  - *Urine pH 6.5*
  - *Urine AG +120*

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Course and Work up

- Continued on broad spectrum antibiotics and weaned from norepinephrine and oxygen
- Stress dose steroids in setting of possible septic shock and for fetal lung maturation
- Infectious work up including blood and urine cultures, RVP, Lyme titers and Anaplasma titers
- Cardiology consulted
  - *Likely ectopic atrial tachycardia secondary to underlying mechanism*
  - *Recommended transthoracic echocardiogram and CT angiogram of Chest given history of peripartum cardiomyopathy*
- Nephrology consulted in setting of NAGMA
  - *Recommended starting bicarbonate infusion*
  - *Autoimmune work up*
  - *24-hour urine calcium*

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Course Continued:

- Infectious work up negative, TTE and CT Angiography of Chest unremarkable
- Completed 5 day course of ceftriaxone and steroids
- Immunological work up negative including Sjogrens and Rheumatoid Arthritis
- No over the counter or prescribed medications related to RTA
- 24 hour urine calcium unremarkable

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Hospitalization and Follow-up

- Patient symptomatically improved following initiation of bicarbonate infusion and she was transitioned to oral supplementation with potassium supplementation
- Nephrology outpatient clinic follow up:
  - *Bicarbonate supplementation stopped 2 months postpartum with spontaneous correction of acidosis*
  - *Likely pregnancy causing exacerbation of Distal RTA in setting of hypokalemia, Urine pH 6.5, Urine anion gap of +120*

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Clinical Manifestations of RTA

- If patient's have symptoms, can include:
  - *Fatigue*
  - *Loss of appetite*
  - *Increased heart rate*
  - *Tachypnea if more severe acidosis*
  - *Symptoms of hypokalemia including muscle weakness, paralysis, and myalgias*
- Presenting at times with obstructive uropathy in setting of hypercalciuria, high urine pH, and reduced citrate excretion

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Urine Anion Gap

- Acid excreted through NH4 (Ammonium) but this cannot be directly measured
  - *Measure through urine anion gap*

$$U_{AG} = Na + K - Cl$$

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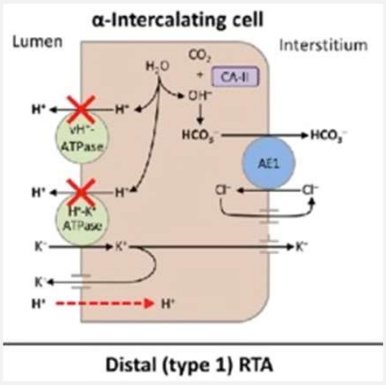

Type 1 Distal Renal Tubular Acidosis

Causes:

- Acquired or inherited
- Autoimmune diseases, hypercalciuria, chemotherapeutic agents, amphotericin B

Pathophysiology:

- Impaired acidification of urine by distal nephron
- Decreased H+ excretion and increased excretion of K+
- Often with significantly lower Bicarbonate levels
- Hypokalemia
- High Urine pH
- UAG positive

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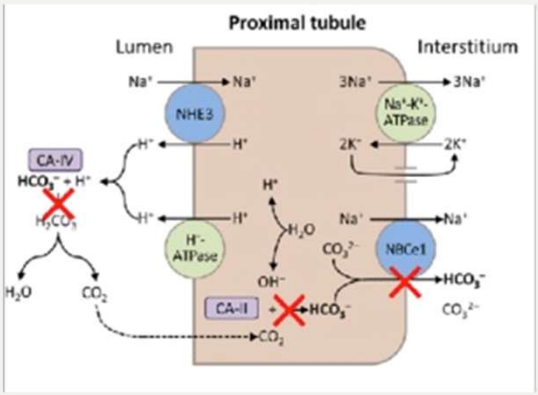

Type 2 Proximal Renal Tubular Acidosis

- Causes:
  - *Fanconi Syndrome (failure of proximal tubule)*
  - *Tenofovir in HIV*
  - *Multiple Myeloma (toxic light chains to PCT)*
  - *Acetazolamide or topiramate use (CA inhibitors)*
- Pathophysiology:
  - *Impaired renal bicarbonate reabsorption in proximal tubule*
  - *Hypokalemia*
  - *Urine pH <5.5 (not associated with kidney stones)*
  - *Negative UAG*

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Type 4 Hyperkalemic Distal Renal Tubular Acidosis

- Causes
  - *Associated with inadequate renal response to aldosterone either through deficiency or resistance*
  - *Addison disease, bilateral adrenalectomy*
- Pathophysiology:
  - *Distal tubule impairs electrolyte transport including sodium, chloride, and potassium*
  - *Bicarbonate typically >17*
  - *Hyperkalemia*
  - *Low urine pH*

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Physiologic Changes in Pregnancy

Cardiac output 30 to 40% above pre-pregnancy levels
Blood volume expansion by 25% resulting in dilutional anemia
Increased Heart Rate
Increased preload due to rise in blood volume
Reduced afterload due to decreased SVR and decreased blood pressure over all
Widened pulse pressure (Nadir around 18 weeks)
Diastolic pressure can be expected to downtrend throughout pregnancy

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Renal Tubular Acidosis Fetal Complications:

- Chronic Metabolic Acidosis in pregnancy complications:
  - *Fetal bone growth and development*
  - *Fetal circulation compromise including fetal distress or demise*
- Pregnancy has been associated with worsening Renal Tubular Acidosis
  - *In pregnancy, mild respiratory alkalosis with urinary bicarbonate loss*
  - *Volume distribution for bicarbonate increases during pregnancy*
  - *Could lead to worsening of RTA however more research is needed*

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Question 1

A 70 year old female presents with fatigue for the last 4 months. She does not take any medications and has no significant past medical history. Routine labs and UA obtained for further work up listed below. What is the most likely cause of the patient's fatigue?

A. Type 1 Distal RTA
B. Type 2 Proximal RTA
C. Type 3 Mixed RTA
D. Type 4 Hyperkalemic Distal RTA

Routine Labs	
Cr	0.9
Na	135
K	3.4
Cl	115
Bicarb	14
Phosphorus	2.1
UA	pH 5, no protein, no blood, trace glucose

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Question 2

76 year old male with history of sarcoidosis, presenting with headaches and lethargy found to have CSF positive for cryptococcal antigen following lumbar puncture. Patient was started on appropriate therapy with amphotericin B and flucytosine. 3 days following induction of therapy, patient noted to have lab findings below. What is the most likely cause of the patient's new lab abnormalities?

A. Type 1 Distal RTA
B. Type 2 Proximal RTA
C. Type 3 Mixed RTA
D. Type 4 Hyperkalemic RTA

Labs	
Cr	0.8
Sodium	136
Potassium	2.8
Chloride	115
AG	10
Bicarbonate	11
Urine pH	6.5

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Which of the following are normal physiologic changes of pregnancy?

A. Increased Cardiac Output, Decreased heart rate, Increased blood volume

B. Increased heart rate, reduced afterload, reduced SVR

C. Narrowed Pulse pressure, increased heart rate, increased preload

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Questions?

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References

- Alkhasoneh M, Jacobs J, Kaur G. A case of severe metabolic acidosis during pregnancy. *Clin Case Rep*. 2019;7(3):550-552. Published 2019 Feb 7. doi:10.1002/ccr3.2042
- Kepley JM, Bates K, Mohiuddin SS. Physiology, Maternal Changes. PubMed. Published March 12, 2023. https://www.ncbi.nlm.nih.gov/books/NBK539766/
- https://www-clinicalkey-com.geihsl.idm.oclc.org/#!/content/clinical_overview/67-s2.0-909a50f2-37d9-42c4-8fff-0ffd6753ab69. 2024 Aug 15.
- Lim VS, Katz AI, Lindheimer MD. Acid-base regulation in pregnancy. *Am J Physiol*. 1976;231(6):1764-1769. doi:10.1152/ajplegacy.1976.231.6.1764
- Palmer, Biff & Kelepouris, Ellie & Clegg, Deborah. (2020). Renal Tubular Acidosis and Management Strategies: A Narrative Review. Advances in Therapy. 38. 10.1007/s12325-020-01587-5.

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