Renal Tubular Acidosis

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Renal Tubular Acidosis:

RTA: is a disease state characterized by a normal anion gap (hyperchloremia) metabolic acidosis in the setting of normal or near-normal glomerular filtration rate.
NORMAL URINARY CIDIFICATION

Kidneys contribute to acid-base balance by reabsorption of filtered bicarbonate (HCO$_3^-$) and excretion of hydrogen ion (H$^+$) produced every day.
pH Control in Kidneys

Blood

H^+

Na^+

HCO_3^-
base

Cells in walls of tubules

H^+ → HCO_3^-

Developing Urine

Na^+ → Na_2HPO_4

Na^+ → NaH_2PO_4

C. Ophardt c. 2005
There are 4 main types

1- Proximal (type II) RTA.

2- Classic distal (type I) RTA.

3- Combined proximal and distal (type III) RTA.

4- Hyperkalemic (type IV) RTA.
PROXIMAL (TYPE II) RENAL TUBULAR ACIDOSIS

PATHOGENESIS

- inherited and persistent
- primary and isolated

Proximal RTA usually occurs as a component of global proximal tubular dysfunction or Fanconi syndrome

- low molecular weight proteinuria
- glycosuria
- phosphaturia
- Aminoaciduria
Causes of pRTA

**Primary**
- Sporadic
- Inherited
  - Inherited renal disease (Idiopathic Fanconi)
  - Sporadic (most common)
  - Autosomal dominant
  - Autosomal recessive
  - X-linked (Dent disease)
  - Inherited syndromes
  - Cystinosis
  - Tyrosinemia type 1
  - Galactosemia
  - Oculocerebral dystrophy (Lowe syndrome)
  - Wilson disease
  - Hereditary fructose intolerance

**Secondary**
- Intrinsic renal disease
  - Autoimmune diseases (Sjogren syndrome)
  - Hypokalemic nephropathy
  - Renal transplant rejection
- Hematologic disease
  - Myeloma
- Drugs
  - Gentamicin
  - Cisplatin
  - Ifosfamide
  - Sodium valproate
- Heavy metals
  - Lead
    - Cadmium
    - Mercury
- Organic compounds
  - Toluene
  - Nutritional
    - Kwashiorkor
- Hormonal
  - Primary hyperparathyroidism

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*Autosomal Recessive Disease

Is caused by mutations in the gene encoding the sodium bicarbonate cotransporter NBC1.

*Autosomal Dominant Disease

has been identified in a single pedigree with nine members presenting with hyperchloremic metabolic acidosis, normal ability to acidify urine, normal renal function, and growth retardation.
Fanconi syndrome

is a disease of the proximal renal tubules of the kidney in which glucose, amino acids, uric acid, phosphate and bicarbonate are passed into the urine, instead of being reabsorbed.

- Polyuria, polydipsia and dehydration
- Hypophosphatemic rickets (in children) and osteomalacia (in adults)
- Growth failure
- Acidosis
- Hypokalemia
- Hyperchloremia

* Other features of the generalized proximal tubular dysfunction of the Fanconi syndrome are:

Hypophosphatemia/phosphaturia
Glycosuria / Proteinuria/aminoaciduria / Hyperuricosuria
Types

1-Inherited :-

- Cystinosis is the most common
- Wilson's disease (a genetically inherited condition of copper metabolism)
- Lowe syndrome,
- Tyrosinemia (Type I),
- Galactosemia,
- Glycogen storage diseases,
- Hereditary fructose intolerance.

Two forms, Dent's disease and Lowe syndrome, are X linked.
2. Acquired:

It is possible to acquire this disease later in life. Causes include ingesting expired tetracyclines, and as a side effect of tenofovir in cases of preexisting renal impairment. In the HIV population, Fanconi syndrome can develop secondary to use of an antiretroviral regimen containing tenofovir and didanosine. Lead poisoning also leads to Fanconi syndrome.

Monoclonal gammopathy of undetermined significance can also cause the condition. Multiple myeloma is also a known cause.
Cystinosis:

Is a systemic disease caused by a defect in the metabolism of cystine, which results in accumulation of cystine crystals in most of the major organs of the body, notably the kidney, liver, eye, and brain.
The diagnosis: suggested by the detection of cystine crystals measurement of increased leukocyte cystine content

**Treatment of cystinosis** is directed at correcting the metabolic abnormalities associated with Fanconi syndrome or chronic renal failure.
Lowe Syndrome

is a rare X-linked disorder characterized by congenital cataracts, mental retardation, and Fanconi syndrome.
CLINICAL MANIFESTATIONS OF PROXIMAL RTA AND FANCONI SYNDROME

1- Growth failure in the 1st year of life.
2- Polyuria, dehydration (due to sodium loss)
3- Anorexia, vomiting, constipation.
4- Hypotonia.
5- Secondary to phosphate wasting, such as rickets.
Distal (Type I) Renal Tubular Acidosis

PATHOGENESIS

Inherited

Acquired

Distal RTA can result in damaged or impaired functioning of one or more transporters or proteins involved in the acidification process, including the H+/ATPase, the HCO3-/Cl- anion exchangers, or the components of the aldosterone pathway.
Causes of dRTA

Primary
- Sporadic
- Inherited
  - Inherited renal diseases
  - Autosomal dominant
  - Autosomal recessive
  - Autosomal recessive with early-onset hearing loss
  - Autosomal recessive with later-onset hearing loss
  - Inherited syndromes associated with type I renal tubular acidosis
  - Marfan syndrome
  - Wilson syndrome
  - Ehlers-Danlos syndrome
  - Familial hypercalciuria

Secondary
- Intrinsic renal
  - Interstitial nephritis
  - Pyelonephritis
  - Transplant rejection
  - Sickle cell nephropathy
  - Lupus nephritis
  - Nephrocalcinosis
  - Medullary sponge kidney
- Urologic
  - Obstructive uropathy
  - Vesicoureteral reflux
- Hepatic cirrhosis
- Toxins or medications
  - Amphotericin B
  - Lithium
CLINICAL MANIFESTATIONS of dRTA

Distal RTA shares features with those of proximal RTA, including non-anion gap metabolic acidosis and growth failure. However, distinguishing features of distal RTA include nephrocalcinosis and hypercalciuria.
Hyperkalemic (Type IV) Renal Tubular Acidosis

PATHOGENESIS

Impaired aldosterone production (hypoaldosteronism)

Impaired renal responsiveness to Aldosterone (pseudohypoaldosteronism)
Causes of Hyperkalemic RTA

Primary

Sporadic
Genetic
- Hypoaldosteronism
- Addison disease
- Congenital adrenal hyperplasia
- Pseudohypoaldosteronism (type I or II)

Secondary

Urologic
- Obstructive uropathy
- Intrinsic renal/
- Pyelonephritis
- Interstitial nephritis
Systemic /
- Diabetes mellitus
- Sickle cell nephropathy
Drugs
- Trimethoprim/ sulfamethaxazole
- Angiotensin-converting enzyme inhibitors
- Cyclosporine
- Prolonged heparinization
Addison disease
DIAGNOSTIC APPROACH

1- Evaluation of a patient with suspected RTA.
2- Confirm the presence of a normal anion gap metabolic acidosis.
3- Identify electrolyte abnormalities.
4- Assess renal function.
5- Rule out other causes of bicarbonate loss such as diarrhea.
TREATMENT AND PROGNOSIS

The mainstay of therapy in all forms of RTA is bicarbonate replacement.

* Proximal RTA :- up to 20 mEq/kg/24 hr in the form of sodium bicarbonate or sodium citrate solution

* Distal RTA :- The range of 2-4 mEq/kg/24 hr

* Patients with type IV RTA can require chronic treatment for hyperkalemia with sodium-potassium exchange resin (Kayexalate).
Rickets Associated with Renal Tubular Acidosis

Rickets may be present in primary RTA, particularly in type II or proximal RTA. Hypophosphatemia and phosphaturia are common in the renal tubular acidosis, which are also characterized by hyperchloremic metabolic acidosis, various degrees of bicarbonaturia, and, often, hypercalciuria and hyperkcaluria.
Points to Remember

* Renal tubular acidosis (RTA) is a disease that occurs when the kidneys fail to excrete acids into the urine, which causes a person's blood to remain too acidic.

* Without proper treatment, chronic acidity of the blood leads to growth retardation, kidney stones, bone disease, chronic kidney disease, and possibly total kidney failure.

* If RTA is suspected, additional information about the sodium, potassium, and chloride levels in the urine and the potassium level in the blood will help identify which type of RTA a person has.

* In all cases, the first goal of therapy is to neutralize acid in the blood, but different treatments may be needed to address the different underlying causes of acidosis.
Thank you very much