Renal Tubular Acidosis; Types and Lab Findings

Renal tubular acidosis refers to a group of disorders in which metabolic acidosis develops as a result of defects in the kidney's ability to acidify the urine.

Renal tubular acidosis is classified into four forms whereby all these are characterized by a normal anion gap and hyperchloremic metabolic acidosis.

Distal Renal Tubular Acidosis (Type 1)

Renal tubular acidosis type 1 is characterized by impaired secretion of H+ by A-type intercalated cells of the collecting ducts and therefore ammonium. It is suspected in any patient with metabolic acidosis with a normal anion gap(non-anion gap metabolic acidosis) and high urine pH greater than 5.0.

> *A negative gap indicates ammonium is present, and a positive gap indicates ammonium is not present.*

Causes

Major causes of distal RTA in adults are;

- Autoimmune disease such as(Sjögren syndrome, SLE, rheumatoid arthritis, chronic active hepatitis).
- Hypercalciuria ie in hyperparathyroidism.
- Drugs (e.g.lithium,toluene, ifosfamide, amphotericin B) or
- Other diseases (pyelonephritis, Hodgkin disease, amyloidosis, sarcoidosis, medullary sponge kidney, sickle cell disease, Wilson's disease).

Hereditary distal RTA is the most common cause of RTA in children.

Treatment is bicarbonate and citrate.

Laboratory Findings

- High urine pH (>5.3; usually in the 6.5–7 range) regardless of serum bicarbonate concentration.
- Urinary pH below 5.3 generally excludes distal (but not proximal) RTA.
- Urine sodium concentration is typical>25 mEq/L.
- Urine ammonium excretion is reduced and can be estimated indirectly by measurement of the urine anion gap or osmolal gap. This parameter can distinguish patients with distal RTA from those who have normal anion gap metabolic acidosis and hypokalemia due to other causes.
- The blood potassium level is usually low.

- Hyperchloremic acidosis and
- low serum bicarbonate concentration (may be <10 mEq/L).
- The ammonium loading test shows an inability to acidify urine below a pH of 5.3.

Proximal Renal Tubular Acidosis (Type 2)

Proximal renal tubular acidosis results from defective bicarbonate reabsorption in the proximal tubule, causing bicarbonate wasting in the urine.

In a normal person HCO- excretion occurs when the levels exceed 24 to 28 mEq/L. In patients with proximal RTA, there is a lower threshold leading to loss of filtered bicarbonate until serum bicarbonate is very low.

This wasting continues until serum bicarbonate concentration reaches a lower threshold enough to allow all of the filtered bicarbonate to be reabsorbed.

It can be present as an isolated disorder or in association with a generalized proximal tubular dysfunction known as Fanconi syndrome, in which reabsorption of other solutes such as phosphate, glucose, uric acid, and amino acids is impaired resulting in bone demineralization due to phosphate wasting.

Most commonly due to increased excretion of light chains in multiple myeloma and other monoclonal gammopathies.

Causes of proximal Renal Tubular Acidosis

Causes of proximal RTA include

- Drugs (such as gentamycin, valproic acid, carbonic anhydrase inhibitors, ifosfamide, aminoglycosides),
- Heavy metals (e.g., lead, mercury), and
- Vitamin D deficiency.
- Related to other diseases such as multiple myeloma.
- Primary causes of proximal RTA can be idiopathic or familial (e.g., bicarbonate transfer mutations, tyrosinemia, galactosemia, Wilson disease, cystinosis, and carbonic anhydrase type 2 deficiency).

Laboratory Findings

Variable urine pH, depending on whether the patient is treated with alkali therapy or not

Low serum bicarbonate concentration (12–20 mEq/L) with hyperchloremic acidosis.

Intravenous (IV) infusion of sodium bicarbonate (0.5–1.0 mEq/kg/ hour) causes an increase in serum bicarbonate concentration toward normal (18–20 mEq/L) and a rapid increase in urine pH (>7.5) and fractional excretion of bicarbonate (>15–20%).

Treatment;

- Bicarbonate (large amounts needed),
- potassium, and
- thiazide diuretics.

Combined or Mixed RTA (Type 3)

Mixed RTA is most often applied to a rare autosomal recessive syndrome that results from carbonic anhydrase II deficiency and has features of both proximal and distal RTA.

Hyperkalemic Renal Tubular Acidosis (Type 4)

Renal tubular acidosis (RTA) type 4, also called hyperkalemic renal tubular acidosis, is characterized by hyperchloremic metabolic acidosis, hyperkalemia, and decreased urinary NH4+ excretion, usually due to aldosterone deficiency or aldosterone resistance.

This type results from either aldosterone deficiency (e.g., primary adrenal insufficiency, ACE inhibitors, severe illness, inherited disorders) or tubular resistance to aldosterone action (e.g., pseudohypoaldosteronism).

Causes.

Aldosterone resistance due to drugs such as pentamidine, spironolactone,diuretics,calcineurium inhibitors.

Genetic aldosterone resistance ie pseudoaldosteronism

Hypoaldosteronism due to high renin, ie in Addison disease, inhibition of aldosterone secretion by heparin, ACE inhibitors, AT1 receptor.

Hypoaldosteronism due to low renin due to diabetes mellitus, NSAIDs, beta-blockers.

You should suspect type 4 RTA in patients with non-AG metabolic acidosis and hyperkalemia.

Characterized by

- Mild hyperchloremic metabolic acidosis
- Hypoaldosterinism
- Diabetes mellitus.

Note that, type 4 is the common form in adults.

Because of the normal functioning of the H+ ATPase, the urine is approximately acidic.

Major laboratory findings:

- Serum bicarbonate concentration typically >15 mEq/L,
- Urine pH <5.3 due to normal ability to secrete hydrogen ions.
- Increased plasma potassium.

Treatment.

- Lower serum potassium (diet, change medications, diuretics).
- Add bicarbonate and fludrocortisone (if aldosterone deficient) but use caution because it causes edema.
- In these patients correction of hyperkalemia leads to a correction of metabolic acidosis.