Autosomal recessive distal renal tubular acidosis with secondary nephrogenic diabetes insipidus in newborn a case report

SENTHIL KUMAR K KALYANASUNDARAM
Department of Neonatology,
MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL

Abstract:
Renal tubular acidosis (RTA) with secondary nephrogenic diabetes insipidus is a rare disease in newborns. Renal tubular dysfunction should be considered as a differential diagnosis in babies who fail to thrive with dehydration, polyuria, hypokalemia and normal anionic gap metabolic acidosis. We present here a case of a term neonate with distal RTA and secondary nephrogenic diabetes insipidus who was successfully managed with intravenous fluids, potassium citrate and thiazide.

Keyword: Renal tubular acidosis, nephrogenic diabetes insipidus, neonate.

Case Report:
28 days old term boy presented with lethargy, poor feeding and tachypnea of two days duration. There was no history of diarrhea or vomiting. Baby had similar complaints two weeks back and was treated with intravenous fluids elsewhere. Family history revealed previous two sibling deaths of second and third born) at two years of age with similar complaints due to renal tubular acidosis. This baby is the 4th born of second degree consanguinous parents and the first born is now a 12 year old healthy boy. There was no history of deafness in the family. The fetal period of this baby was uneventful and there was no polyhydramnios. On examination the baby was lethargic, pale and severely dehydrated (weight loss - 22%) with acidic breathing. The cardiovascular system, abdomen and genitals were clinically normal. Marked hypotonia was observed. Hearing was normal. Skin pigmentation was normal. The infant was found to have polyuria (urine output 7ml/kg/hr) in spite of dehydration.
Figure: 1 Infant with failure to thrive
Blood biochemistry revealed prerenal azotemia, hypernatremia, hypokalemia and high blood osmolality (315 m-osm/kg). Arterial blood gas analysis

Investigations:
showed normal anion gap metabolic acidosis with hyperchloremia. Hemogram showed severe anemia with reticulocytosis indicating hemolysis. Septic screen was normal. The constellation of features like failure to thrive, dehydration with polyuria, absence of diarrhea and normal anion gap acidosis made us to think of renal tubular acidosis (RTA) and second line investigations were planned to confirm the type of RTA and the cause for persistent hypernatremia. His urine pH was alkaline and urine anion gap was positive. Further urine osmolality was low (239 m-osm/kg) and hypercalciuria was present. The fractional excretion of bicarbonate was normal (FEHCO3 < 5%), trans tubular potassium gradient (TTKG >12) was elevated and the baby was unable to concentrate urine after the Vasopressin test.

Figure: 2 USG abdomen- showing nephrocalcinosis of kidney
Ultrasound abdomen showed bilateral medullary nephrocalcinosis. Urine screening for metabolic disorders and the chest x ray were normal. A Diagnosis of Autosomal recessive type 1 RTA with secondary nephrogenic diabetic insipidus was made. Baby was treated with appropriate fluid, bicarbonate correction, potassium citrate supplements, thiazide and other supportive management.

Discussion
Renal tubular acidosis (RTA) is a clinical state of systemic hyperchloremic metabolic acidosis resulting from impaired urinary acidification. Three types exist: Type I-distal RTA (d-RTA) is caused by diminished acid secretion in the distal tubule. Type II -proximal RTA is caused by a reduction in the threshold for bicarbonate resorption in the proximal tubule. Type IV (hyperkalemic) RTA is due to mineralocorticoid deficiency. All the types of RTA are associated with a normal anion gap metabolic acidosis (1). Clinical manifestations of distal RTA include failure to thrive, polyuria, dehydration, muscle weakness, nephrocalcinosis and nephrolithiasis (2, 3).
The diagnosis of distal RTA (2, 3) is based on the following:

(i) Normal anion gap hyperchloremic metabolic acidosis

(ii) Hypokalemia (TTKG > 12 – indicates renal loss of potassium) (4)

(iii) Urine pH greater than 5.5 during acidosis. (FEHCO3 < 5% - indicates normal proximal tubular bicarbonate absorption) (4)

(iv) Positive urinary anion gap (indicates distal renal acidification defect) (4).

(v) Nephrocalcinosis and hypercalciuria

Currently acid loading and alkali loading tests are not mandates for diagnosis of distal RTA (3). Our case presented with all the above classical clinical and biochemical features of distal renal tubular acidosis. But, instead of hyponatremia in distal RTA, our baby had persistent hypernatremia. Further workup revealed hypernatremia with low urine and high blood osmolality and inability to concentrate urine with vasopressin. All of these points towards nephrogenic diabetes insipidus secondary to nephrocalcinosis (5,6). Linshaw MA (6) in his review on nephrogenic diabetes insipidus showed nephrocalcinosis as a secondary cause of diabetes insipidus in infants. Causes of distal RTA may be congenital or acquired. The following are the types of congenital distal RTA (7,8,9).i) Autosomal dominant distal RTA.ii) Autosomal recessive distal RTA - Metabolic acidosis with hemolytic anemia.iii) Autosomal recessive distal RTA with deafness.iv) Autosomal recessive distal RTA without or with late-onset deafness. Acquired distal RTA is due to immunologic destruction of the alpha intercalated cells (eg.amphotericin B).

In our case, the second degree consanguinity, previous two affected siblings, the early onset of disease and the hemolytic anemia in the infant with normal hearing confirm the diagnosis of autosomal recessive distal RTA. The management goals of d-RTA therapy are to improve growth, prevent nephrocalcinosis, nephrolithiasis and prevent renal insufficiency (2). Our baby was treated with fluids for correction of dehydration, bicarbonate and potassium citrate supplementation (5meq/kg/day) for correction of acidosis, potassium supplementation for management of hypokalemia and thiazide for nephrogenic diabetic insipidus. Linshaw MA (6) in his review on nephrogenic diabetes insipidus, the therapy for nephrogenic diabetes insipidus include replacement of fluids, restriction of sodium intake and pharmacologic therapy, including thiazide, amiloride, and indomethacin (6,10).

The baby requires a lifelong treatment with alkali therapy (2) and follow-up for complications like nephrocalcinosis, rickets and renal failure. Untreated, undiagnosed RTA obviously carries a poor outcome, often progressing to end-stage kidney failure from nephrocalcinosis (11).

WHAT THIS CASE REPORT ADDS?

Presence of hypernatremia in a case of distal renal tubular acidosis may be due to associated nephrogenic diabetes insipidus secondary to nephrocalcinosis.

Conclusion:

Failure to thrive in the neonatal period is a challenging clinical condition and there could be many causes for it. Proper history and examination and right workup...
would give a clue to the appropriate diagnosis. Distal renal tubular acidosis is one of the important causes of failure to thrive in neonates and needs careful evaluation. If handled properly, these babies can have a fairly good quality life.

Bibliography

1 Steven Alan Ringer. Renal Tubular Acidosis. NeoReviews 2010;11:252-256


9 Alper SL. Familial renal tubular acidosis. J Nephrol. 2010;23:S57-S76