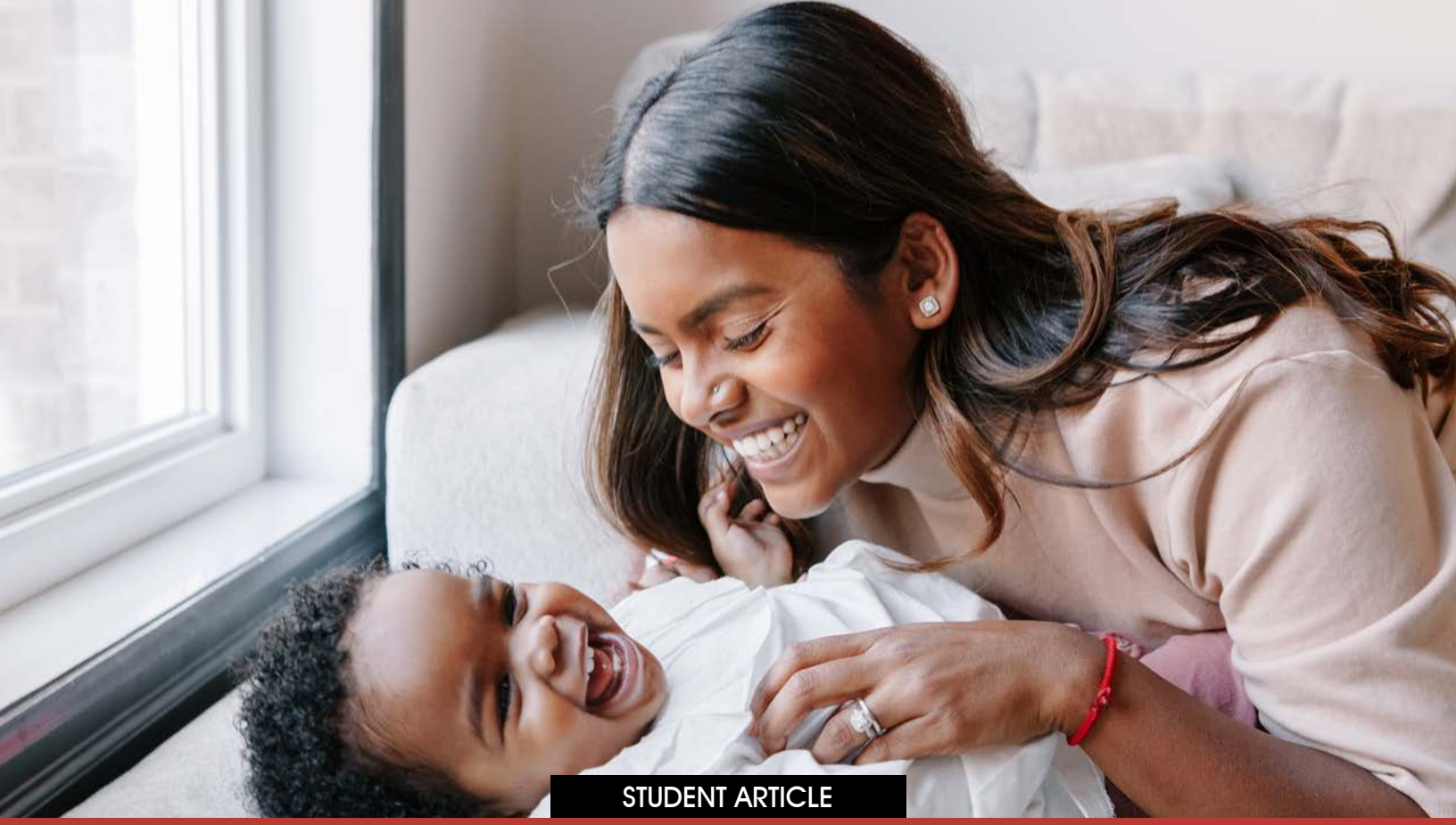

STUDENT ARTICLE

Poor Growth in an 8-month-old Infant: Don't Forget the Kidneys!

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CASE PRESENTATION

An 8-month-old female with a past medical history significant for milk protein allergy presented to clinic with a chief complaint of poor weight gain. At two months of age her weight was at the 30th percentile on the World Health Organization (WHO) Child Growth Standards, but as shown in Figure 1, she dropped to the 6th percentile. The infant's diet consisted of Nutramigen®, 24 Kcal/ounce, 2 to 3 ounces per feed for a total of 15 to 18 ounces daily. She had also been started on pureed fruits and vegetables. Previous attempts at increasing her weight include changing to Alimentum® formula, increasing the caloric density of the formula, and feeding therapy; however, none have made any significant improvement in weight gain over the last six months.

In regard to her history, the pregnancy was notable for intrauterine growth restriction, born at the 4th percentile with oligohydramnios. She was born to a 31-year-old mother (Gravida 2, Para 1) at 38 weeks and 3 days gestation by cesarean section due to a non-reassuring fetal heart rate tracing. She was admitted to the neonatal intensive care unit (NICU) for temperature instability and possible sepsis. However, all testing was reassuring, and she was discharged after three days with no issues. She was diagnosed with cow's milk protein allergy at 4 weeks of life after having bloody streaks in her stool. Since then, she was on Nutramigen® formula and doing well until the latest presentation.

Family history is notable for adult-onset hypertension in her father and maternal grandmother. The maternal grandmother has a history of renal calculi, and the mother has sickle cell trait. There is no family history of short stature, growth issues, or other renal diagnoses. The patient lives with her mother and father in a household with no pets or smokers. She does not attend daycare.

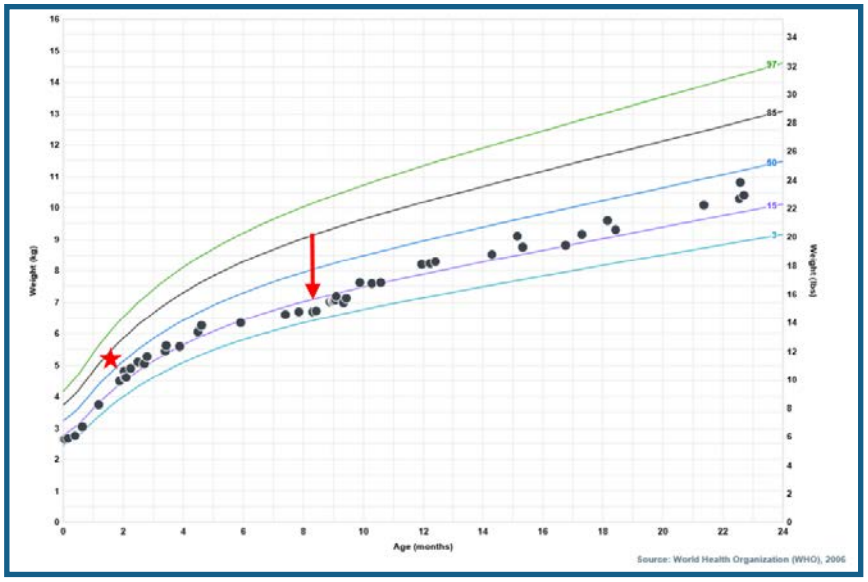

Figure 1. WHO Birth to age 2 years growth chart for our patient Star indicative of 2-month weight at 30th percentile. Arrow indicative of 8-month weight at 6th percentile at time of diagnosis and treatment initiation.

On examination, her weight was 7.025 kg (3rd percentile), height 68 cm (20th percentile), with Z-score of --2.52. Physical exam was unremarkable. Complete metabolic panel was significant for a bicarbonate of 16 mEq/L (18-25 mEq/L) with a normal anion gap. Urinalysis demonstrated a pH of 7 (normal 4-9) and urine electrolytes were sodium 21 mEq/L (normal 20-40 mEq/L), potassium 82.8 mEq/L (normal 25-125 mEq/L) and chloride 27 mEq/L (normal 20 mEq/L). The urine anion gap was +77 (nrmal = 0). She was diagnosed with renal tubular acidosis (RTA), most probably type 1, or distal RTA. A renal ultrasound showed normal kidneys without hydronephrosis, renal calculi, or other abnormalities.

DISCUSSION

Poor weight gain and malnutrition can be difficult to evaluate due to numerous diagnoses within the differential. Many organic disease processes, as well as social and environmental factors, must be considered and fully evaluated.[1] Renal tubular acidosis is a rare cause of poor growth, and in contrast to the adult form, is typically due to a genetic defect in children.[2] RTA is a group of disorders characterized by the inability of proximal renal tubules to reabsorb bicarbonate and distal renal tubules to excrete hydrogen ions, which leads to a primary metabolic acidosis with normal anion gap.[3] The three subtypes of RTA have different pathophysiologies due to genetic mutations or acquired disorders, but they all lead to a hyperchloremic, normal anion gap metabolic acidosis.

In children, the most common forms of RTA are characterized as type 1 (distal tubule) and type 2 (proximal tubule). Classic presenting symptoms in children include vomiting, diarrhea, constipation, poor weight gain or malnutrition (previously referred to as failure to thrive), and rickets.[2] A major concern in pediatric RTA patients is growth restriction.

Type 1, or distal renal tubular acidosis, is due to the inability of the distal tubule and collecting duct to properly excrete acid as hydrogen ions in response to the body's daily acid production. This results in a urine pH above 5.5 and to a positive urine anion gap.[2,4] There are genetic and acquired causes of type 1 RTA that can be autosomal dominant (often less severe cases) or recessive (often more severe) with or without deafness. Two other disorders that can cause a secondary type 1 RTA include Ehlers-Danlos syndrome and sickle cell anemia. Acquired cases may be due to medications, autoimmune disorders, or obstructive uropathy.[4,5]

In contrast, type 2 or proximal RTA is caused by a failure of bicarbonate reabsorption in the proximal tubule leading to excessive urinary loss of bicarbonate. Since distal acidifying mechanisms are appropriately functioning in type 2 RTA, urine is properly acidic if serum bicarbonate levels are low, and urine pH can be below 5.5. However, if serum bicarbonate levels rise to normal levels or above, the proximal tubule cannot properly reabsorb the bicarbonate. The distal tubule is not accustomed to such high levels of bicarbonate and cannot compensate. Thus, urine can be highly alkaline with high bicarbonate excretion.[5] Type 2 RTA can be primary or can simultaneously occur with other proximal tubular defects, in which case it is termed Fanconi syndrome. Isolated type 2 RTA is uncommon and usually transient or associated with another disorder.[2,5]

Type 4 hyperkalemic RTA is much less common, especially in children. It is due to inability to produce ammonia due to hyperkalemia. Urinary pH is normal in response to acidosis, and bicarbonate reabsorption is slightly reduced, but not to the same extent as with a proximal defect. Type 4 RTA can be seen with a number of causes of hyperkalemia, including aldosterone deficiency.[5]

In children, as in the case we have presented, renal tubular acidosis, and specifically type 1 RTA, is more commonly a primary disorder. A thorough family history should be obtained, although many forms follow autosomal recessive transmission, and thus the child may be the first in the family diagnosed with the disease. Three genes have been identified in distal RTA: ATP6V1B1, ATP6V0A4, and SLC4A1, the last of which can be seen as either an autosomal dominant or recessive inheritance.[2] Other symptoms include vomiting, dehydration, polyuria, hypokalemia, hypercalciuria, and hypocitaturia.[1] These cases are also associated with sensorineural deafness.[2]

Though being a complex condition to diagnose, treatment for types 1 and 2 RTA is very rewarding. Consultation with a nephrologist to aid with treatment is highly recommended. Alkali therapy through sodium bicarbonate or a Shohl solution containing citric acid and sodium citrate are appropriate corrective therapies. A newer form of alkali therapy in the form of granules has been approved in Europe and is currently under study in the U.S. for type 1 RTA. Growth and serum bicarbonate level should be regularly monitored in the first 6 months to ensure proper dosing and to rule out other diseases. It is recommended to regularly image the kidneys by ultrasound to monitor for nephrocalcinosis seen in type 1 RTA. Studies have demonstrated various response rates to therapy, with some patients' growth returning to the curve in a few months, and others taking a number of years or not improving at all. Therapy can often be discontinued after resolution of metabolic acidosis, although regular monitoring is vital to ensure no complications arise.[3]

CONCLUSION

Our patient was started on potassium citrate suspension 4 mEq orally given 4 times daily in order to correct for both her acidosis and hypokalemia. At discharge, her acidosis had resolved, and she was gaining weight at a rate above 45g per day. Her weight recovered over the following months and has since remained at the 20th percentile for age. A repeat blood test one week after discharge revealed a normal serum bicarbonate level. At 18 months of age, it was determined that her weight gain and controlled acidosis warranted a trial of weaning off the potassium citrate solution. At the point of discontinuation, the metabolic acidosis returned within one month. Potassium citrate solution was reinstituted with ongoing primary care and nephrology follow up. She was thriving well and developmentally normal at her last visit at 23 months of age.

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