A 2-Month-Old Female Infant with Failure to Thrive

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A 2-month-old previously healthy female infant born at full term presented to the emergency department with increasing difficulty breathing for the past 4 days. On triage, the patient did not have any significant findings and was sent home on supportive measures. The next day, the patient was taken to her primary care physician’s office by her mother for increased difficulty in breathing, increasing fussiness, decreased feeding, and an episode of non-bilious and nonbloody vomiting. During that assessment, the pediatrician noted poor weight gain in the interim since the prior visit. In the office, the patient was found to be normothermic, hypertensive, tachypneic, tachycardic, hypoxic, and profoundly anemic. The patient was subsequently admitted to the hospital.

Her respiratory status continued to worsen, so she was transferred to the pediatric intensive care unit. The patient was subsequently intubated and received supportive measures. There was no known family history of pulmonary, cardiac, renal, neurological, or gastrointestinal problems. The patient lived at home with her nonconsanguineous parents and they denied any exposure to toxic chemicals, pets, or smoke. The patient’s newborn screenings were normal and immunizations were up to date. Physical exam findings of note were pallor, acute respiratory distress as evidenced by a right preauricular pit, and sunken anterior fontanelle.

Figure 1. Sagittal ultrasound view of the patient’s left (a) and right (b) kidneys at day of life 100. The white arrows in both figures are pointing to the hyperechoic regions of the kidneys, suggesting extensive calcification.

For diagnosis, see page 192

Editor’s note: Each month, this department features a discussion of an unusual diagnosis in genetics, radiology, or dermatology. A description and images are presented, followed by the diagnosis and an explanation of how the diagnosis was determined. As always, your comments are welcome via email at Pediatrics@Healio.com.
Case Challenge

**Diagnosis:**

Primary Hyperoxaluria Causing Cortical Nephrocalcinosis

The two main types of hyperoxaluria are primary and secondary. The latter is usually due to enteric causes. Primary hyperoxaluria is a very rare autosomal recessive disease affecting 1 to 2 people per 1 million, and it may be associated with severe renal disease early in life. In this case, genetic testing confirmed the diagnosis of primary hyperoxaluria type I, in which there is a deficiency of the enzyme alanine-glyoxylate aminotransferase. This enzyme is normally found in hepatic peroxisomes and is responsible for converting glyoxylate to glycine. A lack of this enzyme results in the accumulation of insoluble calcium oxalate salts in various tissues, including the kidneys (nephrocalcinosis). Thereafter, end-stage renal disease and systemic oxalosis ensues.

Nephrocalcinosis is defined as the deposition of calcium in the parenchyma of the kidney in either a cortical or medullary distribution. Medullary nephrocalcinosis is much more common than cortical nephrocalcinosis; it usually develops gradually and is an incidental finding on radiographs. The differential diagnosis for cortical nephrocalcinosis includes acute cortical necrosis, chronic glomerulonephritis, hyperoxaluria, chronic transplant rejection, and Alport’s syndrome.

Radiographic findings of cortical nephrocalcinosis include peripheral band of calcification, parallel tram-track line calcification, or diffusely distributed punctuate calcifications representing calcified cortical glomeruli and tubules. Sonographically, there is increased echogenicity present, which may produce acoustic shadowing depending on the amount of calcification. The degree and rapidity of cortical nephrocalcinosis is very evident in both Figure 1 (see page 191) and Figure 2. On computed tomography (CT), one will see punctate band or tram-line calcification in the cortex. CT is the most sensitive radiographic modality for detecting nephrocalcinosis. In Figure 3, one can see that the non-contrast CT image shows uniformly hyperdense renal cortices. On magnetic resonance imaging (MRI), calcifications appear hypointense due to signal voiding in both T1- and T2-weighted scans. Hence, minor calcifications are easily missed on MRI.

A definitive diagnosis of primary hyperoxaluria is made either from genetic sequence blood testing or liver biopsy in which enzymatic activity level is measured. The treatment for this condition involves sequential liver and kidney transplantation. Kidney transplantation alone will not be adequate because the
grafted kidney will still be subject to oxalate deposition. Other treatment options include dialysis, decreasing dietary oxalate consumption, increasing urine output to minimize oxalate deposition using thiazide diuretics due to its calcium retaining properties, and, in some instances, pyridoxine supplementation to promote normal conversion of glyoxylate to glycine.

In this case, the patient presented with profound renal failure and its inherent complications. Upon admission, the patient was hyperkalemic, hypocalcemic, hyperphosphatemic, and had pH and HCO3(−) levels of 6.9 and < 5 mEq/L, respectively. The patient’s blood urea nitrogen and creatinine levels were 162 mg/dL and 13.4 mg/dL, respectively. Based on the method developed by Schwartz and Work, the patient’s calculated glomerular filtration rate was 1.75 mL/min/1.73 m². Due to renal failure suggested by lab data and renal ultrasounds, she was placed on dialysis. Thereafter, serum and urine oxalate level measurements were made. These were 141.1 mcM and 80 mg/day, respectively. These levels, along with other clinical data, prompted us to test for primary hyperoxaluria. This was performed by DNA sequencing of blood samples. Ultimately, a diagnosis of primary hyperoxaluria type I was made.

CONCLUSION

The rapidity and degree of cortical nephrocalcinosis prompted us to test for primary hyperoxaluria. Upon admission, the patient was immediately placed on dialysis and supportive measures. The patient will soon undergo sequential liver and kidney transplantation. While awaiting transplantation, the patient has been placed on an oxalate-restricted diet, thiazide diuretics, and pyridoxine supplementation, in addition to dialysis.

Always keep in mind that in an early infant, rapidly progressing renal failure with cortical nephrocalcinosis is most likely a sign of primary hyperoxaluria.

REFERENCES