PRIMARY HYPEROXALURIA TYPE 1 (PH1)

Navigating the challenges and importance of continued PH1 management[1]

HYPOTHETICAL PATIENT PROFILE:
A 1-year-old patient is diagnosed with PH1 following the diagnosis of his brother.

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This case study is hypothetical and is not representative of all patients with PH1.

PATIENT TIMELINE:

Hypothetical patient profile: A 1-year-old patient is diagnosed with PH1 following the diagnosis of his brother.

PATIENT HISTORY:

AGE 1: PEDIATRIC NEPHROLOGY VISIT

- Patient's older brother was diagnosed with PH1
- Patient is brought to the family's pediatric nephrologist for evaluation of potential PH1[3]

CONFIRMATION OF PH1

PH1 DIAGNOSIS

- Genetic test identified homozygous *AGXT* mutation, confirming PH1[5*]
  *It is recommended that siblings be screened.[4,6]
- Kidney function at time of diagnosis is normal[4,7]

SPOT URINE FINDINGS:
Oxalate:creatinine ratio: 900 mmol/mol[3,4]

IMAGING FINDINGS:
Increased medullary echogenicity suggestive of nephrocalcinosis on ultrasound[4,8]

MEDICAL MANAGEMENT PLAN ESTABLISHED[1,3]:
Water (1.3 L/day), potassium citrate (0.9 g/day), pyridoxine (B6) (45 mg/day)[†]
[†]For an infant who weighs 20 pounds and is 29 inches high.

MANAGEMENT CHALLENGES:

- Due to age, patient needs a gastrostomy tube (G-tube) to enable sufficient fluid intake[1]
- Pyridoxine discontinued 6 months later, following dose escalation, due to lack of effect[3]

ONGOING MANAGEMENT

MONITORING REGIMEN:

- Serum creatinine and urinary oxalate, citrate, and magnesium monitored quarterly[4]
- Twice-yearly ultrasound to monitor stone formation[4]
- Height and weight percentiles followed closely[9]

MANAGEMENT CHALLENGES:

- Caregiver expresses difficulty managing regular G-tube changes and challenges with frequent accidental tube dislodgements[10]
- Caregiver is unable to complete 24-hour urine collection for ongoing urinary oxalate monitoring, so Oxalate:creatinine ratio continues to be assessed in spot urine samples[4,11]

eGFR DECLINES DUE TO DEHYDRATION[12-15]

REPEATED DIARRHEA SECONDARY TO ANTIBIOTIC PROPHYLAXIS[1]

- Presents to emergency department twice in 1 year[1]
- Intravenous fluids administered both times to restore urinary dilution[3]

SPOT URINE FINDINGS:
Oxalate:creatinine ratio: 1100 mmol/mol[4]

IMAGING FINDINGS:
Multiple bilateral stone formation detected[4]

EVOLVING MANAGEMENT:

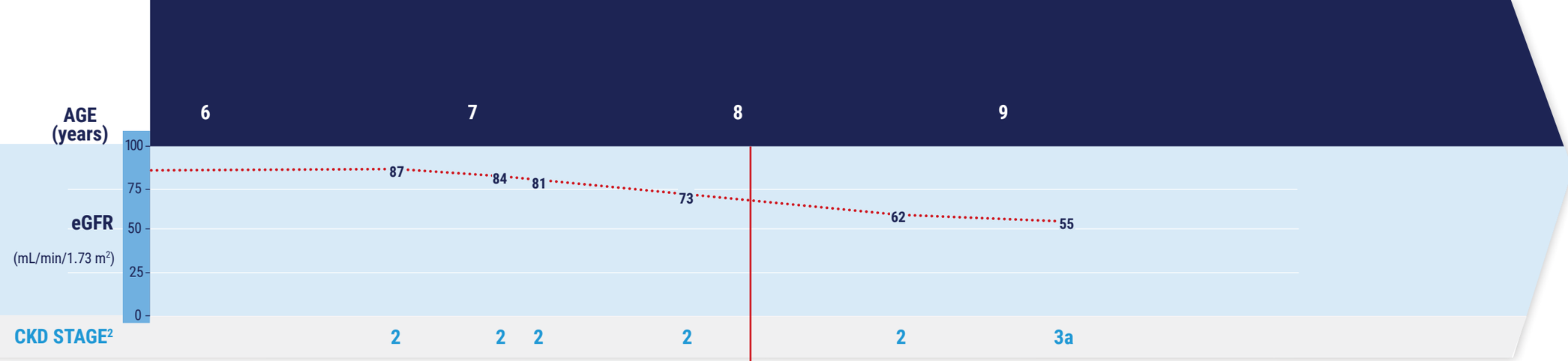
- Water: increased to 1.9 L/day to factor in patient growth[3]
- G-tube is removed[1]

AGXT, alanine glyoxylate aminotransferase; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

Normal spot urinary Oxalate:creatinine values: 7 months-2 years, <132-174 mmol/mol (<0.103-0.136 mg/mg); 2-5 years, <98-101 mmol/mol (<0.076-0.079 mg/mg); 5-14 years, <70-82 mmol/mol (<0.055-0.064 mg/mg)[4]

PATIENT TIMELINE:

Hypothetical patient profile: A 1-year-old patient is diagnosed with PH1 following the diagnosis of his brother.



MANAGEMENT UPDATE

EVOLVING MANAGEMENT:
Water: increased to 2.4 L/day[4] due to factoring in patient growth

SPOT URINE FINDINGS:
Oxalate:creatinine ratio: 1100 mmol/mol[4]

IMAGING FINDINGS:
Worsening nephrocalcinosis reported on ultrasound[4]

MANAGEMENT CHALLENGES:
- Caregiver continually attempts to identify strategies to improve compliance with hydration regimen[1]
- Caregiver expresses challenge of ensuring full oral intake of citrate due to taste aversion[1]

CONFIRMED KIDNEY STONES[3,16]

INCREASED STONE BURDEN
Ongoing monitoring of stones reveals multiple stones increased in size[4]

REFERRAL TO SURGERY:
Patient undergoes surgical removal of complex kidney stones[3]

PATIENT'S MONITORING REGIMEN IS UPDATED TO INCLUDE MORE FREQUENT KIDNEY FUNCTION ASSESSMENTS[4]

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

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TAKEAWAYS:

Genetic testing can be one way to help establish a PH1 diagnosis prior to symptom presentation. Regardless of status of kidney function, genetic testing can help establish a PH1 diagnosis.[3,17-19]

PH1 may cause progressive damage to the kidneys. One of the most devastating aspects of PH1 is that it can progress and culminate in end-stage kidney disease (ESKD).[5,6,19]

Consistent management is key to slowing progression. Management strategies may lessen damage by reducing stone formation and kidney deposition of calcium oxalate crystals.[5,6,20]

PH1 is a very heterogeneous disease. Even siblings with the same genotype experience distinct and variable clinical manifestations.[21]

Consider genetic testing for your patients

when you suspect PH1[5,22]

ONE OPTION FOR TESTING IS THE ALNYLAM ACT® PROGRAM:
Third-party genetic testing and counseling programs offered at no charge to patients.

AlnylamAct®

The Alnylam Act® program was created to provide access to genetic testing and counseling to patients as a way to help people make more informed decisions about their health.

- While Alnylam provides financial support for this program, tests and services are performed by independent third parties
- Healthcare professionals must confirm that patients meet certain criteria to use the program
- Alnylam receives de-identified patient data from this program, but at no time does Alnylam receive patient-identifiable information. Alnylam may use healthcare professional contact information for research purposes
- Both genetic testing and genetic counseling are available in the US and Canada
- Healthcare professionals or patients who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use, or support any Alnylam product
- No patients, healthcare professionals, or payers, including government payers, are billed for this program

FOR MORE INFORMATION, VISIT ALNYLAMACT.COM AND ABOUTPH1.COM >

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