PRIMARY HYPEROXALURIA TYPE 1 (PH1)

Prompt and continued management is key in PH1[1]

HYPOTHETICAL PATIENT PROFILE:

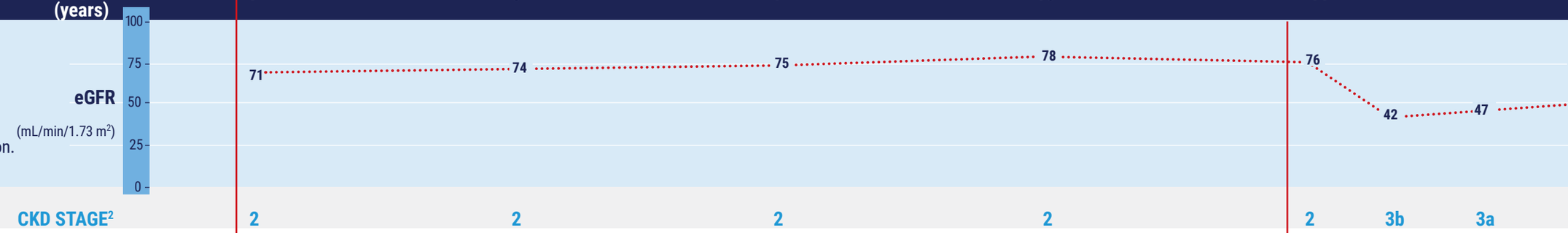
A pediatric patient experiences a rapid and progressive decline in kidney function.

BEHIND THE STONE

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

PATIENT TIMELINE:

Hypothetical patient profile: a pediatric patient experiences a rapid and progressive decline in kidney function.



REFERRAL TO PEDIATRIC NEPHROLOGIST

PH1 DIAGNOSIS
- CKD stage 2[2]
- Elevated oxalate confirmed in 24-hour urine analysis[5]

IMAGING FINDINGS:
Increased medullary echogenicity suggestive of nephrocalcinosis on ultrasound[7,9]

GENETIC TEST FINDINGS:
Genetic test identified homozygous *AGXT* mutation, confirming PH1[1]*

*It is recommended that siblings be screened.[5,7]

MEDICAL MANAGEMENT PLAN ESTABLISHED[1]:
Water (2.7 L/day), potassium citrate (2.4 g/day), pyridoxine (B6) (235 mg/day)†

†For a 7-year-old child who weighs 51 pounds and is 3 feet 9 inches high.

KIDNEY FUNCTION STABLE WITH ONGOING MANAGEMENT[1,7]

MONITORING REGIMEN:
- Serum creatinine and urinary oxalate, citrate, and magnesium monitored quarterly[7]
- Twice-yearly ultrasound to monitor stone formation[7]
- Height and weight percentiles monitored closely[10]

24-HOUR URINE FINDINGS:
Oxalate[5]: 2.4 mmol (211.2 mg)/24h/1.73 m²

EVOLVING MANAGEMENT:
- Water: increased to 3 L/day to factor in patient growth[11]
- Potassium citrate: continue at 0.1 g/kg/day[1]
- Pyridoxine: increased to 15 mg/kg/day due to unclear response (<30% decrease in 24-hour urinary oxalate)[1]

IMAGING FINDINGS:
Bilateral stone development detected[7]

24-HOUR URINE FINDINGS:
Oxalate[5]: 2.3 mmol (202.4 mg)/24h/1.73 m²

eGFR DECLINES DUE TO DEHYDRATION[7,12]

PATIENT CONTRACTS THE FLU[12]
Intravenous fluids administered to restore urinary dilution[1]

PATIENT HISTORY:

AGE 3: PEDIATRICIAN VISIT
Brief episode of nausea, vomiting, and irritability accompanied by abdominal pain[3,4]

AGE 7: ED VISIT
KIDNEY STONE EVENT
Episode of gross hematuria associated with 3-mm kidney stone that resolved nonsurgically[4-6]

STONE ANALYSIS:
Stone composed of calcium oxalate monohydrate[1]

24-HOUR URINE FINDINGS:
Oxalate[5]: 2.7 mmol (237.6 mg)/24h/1.73 m²

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

Normal urinary oxalate level (all ages)[7]: <0.50 mmol (<45 mg)/24h/1.73 m²

Normal plasma oxalate level[8]: 1-5 mmol/L

PATIENT TIMELINE:

Hypothetical patient profile: a pediatric patient experiences a rapid and progressive decline in kidney function.

eGFR REBOUNDS AS PATIENT RECOVERS[11]

EVOLVING MANAGEMENT:
Water: increased to 3.2 L/day[7]

24-HOUR URINE FINDINGS:
Oxalate[5]: 2.1 mmol (184.8 mg)/24h/1.73 m²

KIDNEY STONE EVENT:
Removed endoscopically by urologist

KIDNEY FUNCTION CONTINUES TO DECLINE DESPITE CONSISTENT MANAGEMENT[13]

eGFR DECLINES WITHIN A YEAR

PLASMA OXALATE LEVEL:
15 µmol/L[12]

MONITORING REGIMEN:
- Regular measurement of plasma oxalate due to concern of systemic oxalosis[7]
- Increased frequency of kidney function assessment[7]

PATIENT ADDED TO NATIONAL TRANSPLANT WAITING LIST FOR COMBINED LIVER/KIDNEY TRANSPLANT[1]

CKD, chronic kidney disease;
eGFR, estimated glomerular filtration rate;
ESKD, end-stage kidney disease.

Normal urinary oxalate level (all ages)[7]:
<0.50 mmol (<45 mg)/24h/1.73 m²

TAKEAWAYS:

Urolithiasis is unusual in children. Consider investigating the possibility of a genetic cause when a child presents with any stone event.[7]

PH1 typically results in progressive decline in kidney function. Monitoring for decline in kidney function may be needed. In some instances, kidney function can decline after a single incident of dehydration due to acute illness or intense physical activity. This can occur even in patients with previously stable kidney function.[5,7,12,14,15]

Active management of PH1 may help slow the progression to ESKD. However, some patients may eventually progress to ESKD when a combined liver/kidney transplant is their only option. This procedure carries significant long-term morbidity and mortality risks.[5,7,13,16]

PH1 is a very heterogeneous disease. Even siblings with the same genotype experience distinct and variable clinical manifestations.[18]

Consider genetic testing for your patients

when you suspect PH1[16,19]

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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