

PRIMARY HYPEROXALURIA TYPE 1 (PH1)

Navigating the challenges and importance of continued PH1 management¹



HYPOTHETICAL PATIENT PROFILE:

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

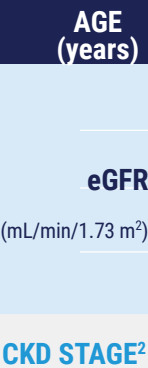
This case study is hypothetical and is not representative of all patients with PH1.

BEHIND THE
STONE



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 PH1³

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

1
100

2

3

4

5

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 intake¹
- Pyridoxine discontinued 6 months later, following dose escalation, due to lack of effect³

ONGOING MANAGEMENT



MONITORING REGIMEN:

- Serum creatinine and urinary oxalate, citrate, and magnesium monitored quarterly⁴
- Twice-yearly ultrasound to monitor stone formation⁴
- Height and weight percentiles followed closely⁹

MANAGEMENT CHALLENGES:

- Caregiver expresses difficulty managing regular G-tube changes and challenges with frequent accidental tube dislodgements¹⁰
- 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 DEHYDRATION¹²⁻¹⁵



REPEATED DIARRHEA SECONDARY
TO ANTIBIOTIC PROPHYLAXIS¹

- Presents to emergency department twice in 1 year¹
- Intravenous fluids administered both times to restore urinary dilution³

SPOT URINE FINDINGS:

Oxalate:creatinine ratio: 1100 mmol/mol⁴

IMAGING FINDINGS:

Multiple bilateral stone formation detected⁴

EVOLVING MANAGEMENT:

- Water: increased to 1.9 L/day to factor in patient growth³
- G-tube is removed¹

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/day⁴ due to factoring in patient growth

SPOT URINE FINDINGS:
Oxalate:creatinine ratio: 1100 mmol/mol⁴

IMAGING FINDINGS:
Worsening nephrocalcinosis reported on ultrasound⁴

MANAGEMENT CHALLENGES:

- Caregiver continually attempts to identify strategies to improve compliance with hydration regimen¹
- Caregiver expresses challenge of ensuring full oral intake of citrate due to taste aversion¹

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

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

CONFIRMED KIDNEY STONES^{3,16}



INCREASED STONE BURDEN
Ongoing monitoring of stones reveals multiple stones increased in size⁴

REFERRAL TO SURGERY:
Patient undergoes surgical removal of complex kidney stones³



PATIENT'S MONITORING REGIMEN IS UPDATED TO INCLUDE
MORE FREQUENT KIDNEY FUNCTION ASSESSMENTS⁴



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.



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](https://alnylamact.com) AND [ABOUTPH1.COM](https://aboutph1.com) >**

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