

PRIMARY HYPEROXALURIA TYPE 1 (PH1)

Prompt and continued management is key in PH1¹



HYPOTHETICAL PATIENT PROFILE:

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

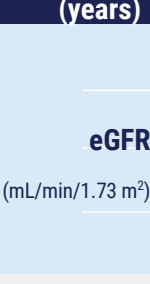
This case study is hypothetical and is not representative of all patients with PH1.

BEHIND THE
STONE

PATIENT
TIMELINE:

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

AGE
(years)



CKD STAGE²

7

8

9

10

11

REFERRAL TO PEDIATRIC
NEPHROLOGIST



PH1 DIAGNOSIS

- CKD stage 2²
- Elevated oxalate confirmed in 24-hour urine analysis⁵

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 ESTABLISHED¹:

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 quarterly⁷
- Twice-yearly ultrasound to monitor stone formation⁷
- Height and weight percentiles monitored closely¹⁰

24-HOUR URINE FINDINGS:

Oxalate⁵: 2.4 mmol (211.2 mg)/24h/1.73 m²



EVOLVING MANAGEMENT:

- Water: increased to 3 L/day to factor in patient growth¹¹
- Potassium citrate: continue at 0.1 g/kg/day¹
- Pyridoxine: increased to 15 mg/kg/day due to unclear response (<30% decrease in 24-hour urinary oxalate)¹

eGFR DECLINES DUE
TO DEHYDRATION^{7,12}



PATIENT CONTRACTS
THE FLU¹²

Intravenous fluids administered to restore urinary dilution¹

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 nonsurgically⁴⁻⁶

STONE ANALYSIS:

Stone composed of calcium oxalate monohydrate¹

24-HOUR URINE FINDINGS:

Oxalate⁵: 2.7 mmol (237.6 mg)/24h/1.73 m²

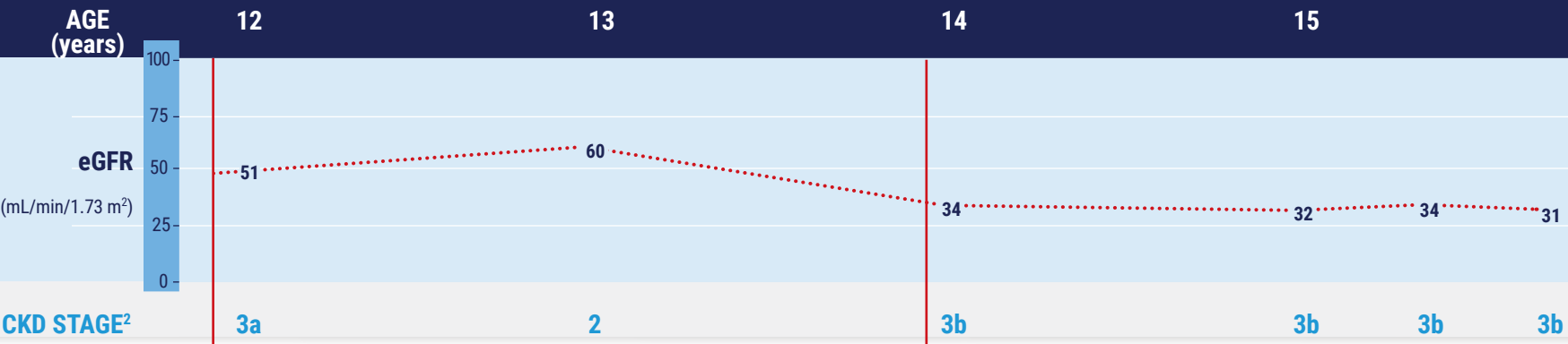
AGXT, alanine glyoxylate aminotransferase;
CKD, chronic kidney disease;
ED, emergency department;
eGFR, estimated glomerular filtration rate.

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

Normal plasma oxalate level⁸: 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 RECOVERS¹¹



EVOLVING MANAGEMENT:
Water: increased to 3.2 L/day⁷

24-HOUR URINE FINDINGS:
Oxalate⁵: 2.1 mmol (184.8 mg)/24h/1.73 m²

KIDNEY STONE EVENT:
Removed endoscopically by urologist

KIDNEY FUNCTION CONTINUES TO DECLINE DESPITE CONSISTENT MANAGEMENT¹³



eGFR DECLINES WITHIN A YEAR

PLASMA OXALATE LEVEL:
15 µmol/L¹²

MONITORING REGIMEN:

- Regular measurement of plasma oxalate due to concern of systemic oxalosis⁷
- Increased frequency of kidney function assessment⁷



PATIENT ADDED TO NATIONAL TRANSPLANT WAITING LIST FOR COMBINED LIVER/KIDNEY TRANSPLANT¹

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

References: 1. Cochat P, Hulton SA, Acquaviva C, et al. *Nephrol Dial Transplant*. 2012;27(5):1729-1736. doi:10.1093/ndt/gfs078 2. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl*. 2013;3(1). 3. NIDDK. Symptoms & causes of kidney stones in children. Accessed February 26, 2020. <https://www.niddk.nih.gov/health-information/urologic-diseases/kidney-stones-children/symptoms-causes> 4. Chu DI, Tasian GE, Copelovitch L. *Curr Treat Options Pediatr*. 2016;2(2):104-111. doi:10.1007/s40746-016-0046-8 5. Hoppe B, Beck BB, Milliner DS. *Kidney Int*. 2009;75(12):1264-1271. doi:10.1038/ki.2009.32 6. Coll DM, Varanelli MJ, Smith RC. *AJR Am J Roentgenol*. 2002;178(1):101-103. doi:10.2214/ajr.178.1.1780101 7. Milliner DS, Harris PC, Cogal AG, Lieske JC. In: Adam MP, Ardinger HH, Pagon RA, et al. *GeneReviews*®. University of Washington, Seattle; 1993-2021. 8. Bhasin B, Ürekli HM, Atta MG. Primary and secondary hyperoxaluria: Understanding the enigma. *World J Nephrol*. 2015 May 6;4(2):235-44. doi: 10.5527/wjn.v4.i2.235. PMID: 25949937; PMCID: PMC4419133. 9. Ferraro PM, D'Addessi A, Gambaro G. *Nephrol Dial Transplant*. 2013;28(4):811-820. doi:10.1093/ndt/gfs545 10. Harambat J, Bonthuis M, van Stralen KJ, et al. *Clin J Am Soc Nephrol*. 2014;9(1):92-99. doi:10.2215/CJN.00890113 11. Fargue S, Harambat J, Gagnadoux M-F, et al. *Kidney Int*. 2009;76(7):767-773. doi:10.1038/ki.2009.237 12. Leumann E, Hoppe B. *J Am Soc Nephrol*. 2001;12(9):1986-1993. doi:10.1681/ASN.V1291986 13. Jamieson NV; European PHI Transplantation Study Group. *Am J Nephrol*. 2005;25(3):282-289. doi:10.1159/000086359 14. Tintillier M, Pochet J-M, Cosyns J-P, Delgrange E, Donckier J. *Clin Nephrol*. 2004;62(2):155-157. doi:10.5414/cnp62155 15. Harambat J, Fargue S, Bacchetta J, Acquaviva C, Cochat P. *Int J Nephrol*. 2011;2011:864580. doi:10.4061/2011/864580 16. Cochat P, Rumsby G. *N Engl J Med*. 2013;369(7):649-658. doi:10.1056/NEJMra1301564 17. Williams EL, Bagg EA, Mueller M, Vandrovicova J, Aitman TJ, Rumsby G. *Mol Genet Genomic Med*. 2015;3(1):69-78. doi:10.1002/mgg3.118 18. Hoppe B. *Kidney Int*. 2010;77(5):383-385. doi:10.1038/ki.2009.471 19. Hoppe B. *Nat Rev Nephrol*. 2012;8(8):467-475. doi:10.1038/nrneph.2012.113

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