TESTING

according to the guidelines on medical management of kidney stones, including those from the American Urological Association (AUA)[1-3]

Utilizing 24-hour urine tests to help diagnose a metabolic stone disease[1]

HYPOTHETICAL PATIENT PROFILE:

Susan

Female | Age 12 | Asian American

Height 5′ 1″ | Weight 42 kg | BMI 17.5 kg/m^2

A young stone former with high oxalate concentration in urine

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

This information is provided for educational purposes only and is not intended to replace the independent medical judgment of any healthcare professional.

PATIENT TIMELINE: First 5 weeks

STONE EVENT & MANAGEMENT

PRESENTING SYMPTOMS[4]

Presented to pediatrician with intermittent pain in the left flank region with occasional nausea/vomiting; without fever or chills. Referred to pediatric urologist

SCREENING EVALUATION

Medical history[1]: No history of stone events

Family history[1]: No familial history of stone formation

Dietary history[1]: No nutritional factors associated with a stone disease; normal fluid intake

Serum chemistry[1]:
- Normal kidney function

Spot urine analysis[1,2,5,6]:
- Normal pH
- No hematuria
- Negative cultures
- Dumbbell-shaped oxalate crystals

DIAGNOSTIC IMAGING

CT scan[1,7]:
- Two left midureteral stones. Size of both stones <8 mm
- Mild bilateral nephrocalcinosis

MANAGEMENT STEPS[1,7]

- No surgical intervention planned due to stone size
- Urologist recommends increasing water intake

STONE PASSAGE

- One stone was collected for analysis
- Follow-up with urologist planned

CT= computed tomography
All CT scan images provided by Dr. David Schulsinger

3 weeks after the stone passage

FOLLOW-UP VISIT WITH UROLOGIST

FOLLOW-UP EVALUATION[8]

Similar results in follow-up serum chemistry and spot urine analyses

STONE ANALYSIS[9]

Stone composition:
Calcium oxalate monohydrate (70%) and dihydrate (30%) mix

DIAGNOSTIC STEPS[1,10,11]

Urologist instructed the patient's caregiver to collect 2 consecutive 24-hour urine samples in the next week while staying on a self-determined diet under normal daily conditions

2 weeks later

METABOLIC WORKUP

24-HOUR URINE TEST RESULTS

- **Results of Sample 1[12]:**
  – Creatinine level: 17 mg/kg/24 h, indicating overcollection
- **Results of Sample 2[12]:**
  – Creatinine level: 12 mg/kg/24 h, indicating proper collection

ANALYTE	PATIENT VALUE	REFERENCE RANGE*
Volume	2.6 L/day	>20 mL/kg/day
Calcium	2.9 mg/day	<4 mg/kg/day
	0.073 mmol/day	<0.1 mmol/kg/day
Oxalate	**85 mg/1.73m^2/24 h**	<45 mg/1.73m^2/24 h
	0.94 mmol/1.73m^2/24 h	<0.5 mmol/1.73m^2/24 h
Citrate	420 mg/1.73 m^2/day	>310 mg/1.73 m^2/day
	2.2 mmol/1.73 m^2/day	>1.6 mmol/1.73 m^2/day
Urate	7.5 mg/kg/day	<9.3 mg/kg/day
	44.4 µmol/kg/day	<55 µmol/kg/day

**Reference ranges assay-dependent and intended to provide a guide for clinicians. Oxalate values are normalized for body surface area (BSA)*

Because oxalate level is >75 mg/day (0.83 mmol/day), urologist suspects primary hyperoxaluria and orders genetic panel for PH1, PH2, and PH3[1-3]

Guidelines recommend genetic testing for PH in patients with elevated urinary oxalate excretion, including those from the AUA, which recommend testing when urinary oxalate excretion is >75 mg/day in adult patients without bowel dysfunction.[1-3]

3 weeks later

DIAGNOSIS OF UNDERLYING CAUSE OF STONE FORMATION

GENETIC TESTING RESULT[2]

Urologist identifies *AGXT* mutations and confirms a diagnosis of primary hyperoxaluria type 1 (PH1)

NEPHROLOGIST CONSULTATION[2]

Urologist sets up a consultation with a nephrologist for ongoing medical management of PH1

TESTING | 3 TAKEAWAYS

- **Performing proper collection of 24-hour urine samples is critical to accurate interpretation of metabolic workup results[13]**
- **Assessing metabolic workup results may help indicate an inherited stone disease, and prompt genetic testing can help confirm PH per guidelines, including AUA[1-3]**
- **Any kidney stone in a child or adolescent merits further investigation to seek an underlying genetic cause[14]**

ACTIONS THAT MAY IMPACT THE DIAGNOSTIC JOURNEY OF A STONE FORMER

IDENTIFICATION
of high-risk factors

TESTING
according to the guidelines on medical management of kidney stones, including those from the American Urological Association (AUA)

CONSULTING
with a nephrologist when warranted

24-hour urine testing in high-risk, recurrent, and interested first-time stone formers, as recommended by guidelines, including those from the AUA, can help identify metabolic stone disease.[3] Consider ordering or referring your patients for genetic testing when you suspect an inherited stone disease such as PH1.[3,15]

ONE OPTION FOR TESTING WHEN YOU SUSPECT PH1 IS THE ALNYLAM ACT® PROGRAM:
Third-party genetic screening and counseling for patients who may have PH1 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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1. Pearle MS, Goldfarb DS, Assimos DG, et al. *J Urol.* 2014;192(2):316-324. **2.** Cochat P, Hulton SA, Acquaviva C, et al. *Nephrol Dial Transplant.* 2012;27(5):1729-1736. **3.** Hoppe B. *Nat Rev Nephrol.* 2012;8(8):467-475. **4.** Brisbane W, Bailey MR, Sorensen MD. *Nat Rev Urol.* 2016;13(11):654-662. **5.** Williams JC Jr, Gambaro G, Rodgers A, et al. *Urolithiasis.* 2021;49(1):11-16. **6.** Edvardsson VO, Goldfarb DS, Lieske JC, et al. *Pediatr Nephrol.* 2013;28(10):1923-1942. **7.** Assimos D, Krambeck A, Miller NL, et al. *J Urol.* 2016;196(4):1161-1169. **8.** Gambaro G, Croppi E, Coe F, et al. *J Nephrol.* 2016;29(6):715-734. **9.** Goldstein R, Goldfarb DS. Urol Nurs. 2017;37(2):81-102. **10.** Ennis JL, Asplin JR. *Int J Surg.* 2016;36(Pt D):633-637. **11.** Ellison JS, Hollingsworth JM, Langman CB. *J Pediatr Urol.* 2017;13(6):632.e1-321.e7. **12.** Chan KH, Moser EA, Whittam BM, et al. *J Pediatr Urol.* 2019;15(1):74.e1-74.e7. **13.** Boyd C, Wood K, Whitaker D, et al. *Rev Urol.* 2018;20(3):119-124. **14.** Ferraro PM, D'Addessi A, Gambaro G. *Nephrol Dial Transplant.* 2013;28(4):811-820. **15.** Cochat P, Rumsby G. *N Engl J Med.* 2013;369(7):649-658.

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