CONSULTING
with a nephrologist when warranted

Consulting with a nephrologist when a metabolic stone disease is suspected[1]

HYPOTHETICAL PATIENT PROFILE:
Michael

Male | Age 28 | Hispanic American | BMI 29 kg/m²

A frequent recurrent stone former with compromised kidney function

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. For U.S. HCPs only.

PATIENT TIMELINE: First Month

STONE EVENT & MANAGEMENT

PRESENTING SYMPTOMS[2]
Referred to urologist by PCP due to increasingly severe bouts of abdominal pain suspected to be renal colic

SCREENING EVALUATION
Medical history[3]: Previous stone event as a young child, resolved without intervention; no record of stone analysis

Dietary history[3]: Normal fluid intake

Serum chemistry[3]:
- Normal eGFR (CKD Stage 1)

Spot urine analysis[3,4]:
- Normal pH
- No hematuria
- Negative cultures
- Calcium oxalate monohydrate crystals

Figure from Daudon, *Clin Chem Lab Med.* 2015; S3 (Suppl): S1479-S1487.[1]

DIAGNOSTIC IMAGING
KUB radiography[3,5]:
- 7-mm right midureteral stone

STONE REMOVAL[6]
URS with laser lithotripsy and stone manipulation; no complications

STONE ANALYSIS[7]
Stone composition: calcium oxalate, >95% monohydrate form

DIAGNOSTIC STEPS[8]
Follow-up imaging planned in 3 months

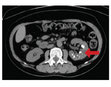
UROLOGIST CONSULTS WITH NEPHROLOGIST[1]
- Reduced eGFR in the absence of stone-related obstruction prompts urologist to consult with a nephrologist

CKD = chronic kidney disease
eGFR = estimated glomerular filtration rate;
KUB = kidney, ureter, bladder;
URS = ureteroscopy

3 months later

RECURRENT STONE EVENT

FOLLOW-UP IMAGING WITH UROLOGIST
CT SCAN[3,6]:
- Multiple instances of new stone formation in both kidneys; patient is asymptomatic
- Evidence of left renal nephrocalcinosis



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

SCREENING EVALUATION
SERUM CHEMISTRY[3]
- CKD Stage 2

SPOT URINE ANALYSIS[3,4]:
Normal except for oxalate/creatinine ratio of 1.1 mmol/mmol (0.875 mg/mg)

UROLOGIST CONSULTS WITH NEPHROLOGIST[1]
Urologist informs nephrologist of continually decreasing eGFR

2 weeks later

STONE MANAGEMENT

UROLOGIST CONSULTS WITH NEPHROLOGIST
Metabolic workup with nephrologist delayed due to recurrent stone event

3 months later

DIAGNOSIS OF UNDERLYING CAUSE OF STONE FORMATION

24-HOUR URINE TEST[3]
- Nephrologist orders and reviews the 24-hour urine test results

ANALYTE	PATIENT VALUE	REFERENCE RANGE*
Volume	2.9 L/day	0.5-4L/day
Oxalate	**153 mg/day (1.7 mmol/day)**	20-40 mg/day (0.22-0.44 mmol/day)
Calcium	148 mg/day (3.7 mmol/day)	male <250 mg/day (<6.25 mmol/day), female <200 mg/day (<5 mmol/day)

*Reference ranges assay-dependent and intended to provide a guide for clinicians

- Nephrologist suspects underlying metabolic stone disease and orders genetic testing[3]

GENETIC TESTING[9]
Genetic testing identifies AGXT mutations and helps confirm a diagnosis of primary hyperoxaluria type 1 (PH1)

Ongoing

UROLOGIST-NEPHROLOGIST CO-MANAGEMENT

ONGOING NEPHROLOGIST AND UROLOGIST PATIENT MANAGEMENT[1,9]
- Nephrologist medically manages the patient
- Urologist continues to be involved in patient care and provides procedural intervention as needed

CONSULTING | 3 KEY TAKEAWAYS

- **Consulting with a nephrologist when treating patients who are stone formers or who are at risk for CKD/ESKD can help diagnose an underlying genetic condition[1]**
- **Ordering a full metabolic workup can be warranted in higher-risk patients with early kidney stone onset and nephrocalcinosis[3]**
- **Collaborating with a nephrologist can help ensure appropriate metabolic workup following stone resolution, and may provide support for ongoing management[1]**

CKD = chronic kidney disease
ESKD = end-stage kidney disease

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)

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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.[1] Consider ordering or referring your patients for genetic testing when you suspect an inherited stone disease such as PH1.[10,11]

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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References:
1. Gambaro G, Coppi E, Coe F, et al. *J Nephrol.* 2016;29(6):715-734. **2.** Brisbane W, Bailey MR, Sorensen MD. *Nat Rev Urol.* 2016;13(11):654-662. **3.** Pearle MS, Goldfarb DS, Assimos DG, et al. *J Urol.* 2014;192(2):316-324. **4.** Williams JC Jr, Gambaro G, Rodgers A, et al. *Urolithiasis.* 2021;49(1):1-16. **5.** Daudon M, Frochot V. *Clin Chem Lab Med.* 2015;53 (suppl 2):s1479-s1487. **6.** Assimos D, Krambeck A, Miller NL, et al. *J Urol.* 2016;196(4):1161-1169. **7.** Goldstein R, Goldfarb DS. *Urol Nurs.* 2017;37(2):81-102. **8.** Khan SR, Pearle MS, Robertson WG, et al. *Nat Rev Dis Primers.* 2016;2:16008. **9.** Cochat P, Hulton SA, Acquaviva C, et al. *Nephrol Dial Transplant.* 2012;27(5):1729-1736. **10.** Cochat P, Rumsby G. *N Engl J Med.* 2013;369(7):649-658. **11.** Hoppe B. *Nat Rev Nephrol.* 2012;8(8):467-475.

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