Primary hyperoxaluria type 1 (PH1) is an ultra-rare, debilitating, inherited condition that typically presents in childhood and is characterized by painful kidney stones, often intractable progression to end-stage kidney disease (ESKD) and increased morbidity and mortality. PH1 is frequently under- or misdiagnosed. Inaccurate diagnoses pose a high risk of irreversible damage.

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PH1 is caused by mutations in the AGT gene that render the liver enzyme alanine-glyoxylate amido transaminase (AGT) dysfunctional. AGT, when functional, helps rid the body of unwanted products of normal metabolism. In people with PH1, defective AGT causes an abnormal accumulation of oxalate—a waste product not used by the body—initially in the kidneys, and, when the disease advances, in other organs.

Role of oxalate in PH1

Even in the absence of overt symptoms, oxalate is constantly being overproduced and can cause irreversible damage to the kidneys.

Oxalate crystals. As nephrocalcinosis occurs, renal impairment causes crystals to be deposited throughout the body, damaging kidneys and major non-kidney organs.

High levels of oxalate are toxic, and crystals can be broken down by the body.

ESKD is a looming threat for people living with PH1

PH1 can ultimately result in ESKD, a life-threatening condition also known as kidney failure that prevents the kidneys from functioning properly. Once kidney function has been compromised, oxalate can spread throughout the body, resulting in systemic oxalosis wherein oxalate crystals can deposit in the eyes, skin, bones, heart and central nervous system of people with PH1.

Consequences of systemic oxalosis include:

- Bone fractures
- Heart failure
- Skin ulcers
- Diminished vision
- Other complications

For example, children, adults and caregivers of those with PH1 experience the anxiety of not knowing:

- When will the next painful kidney stone episode occur?
- How long will their or their loved one’s kidney stones keep working?
- Will they or their child/loved one need to undergo an organ transplant?

Diagnosing PH1

Inaccurate diagnoses pose a high risk of irreversible damage. Given the ultra-rare nature of the disease and symptoms that are often mistaken for that of other conditions, PH1 is frequently under- or misdiagnosed. Early diagnosis is crucial and may allow for appropriate management of symptoms. 1,2,5

Guidelines recommend metabolic testing including 24-hour urine collections. 3\(^5\) Spot urine measurements are not recommended to screen for PH1 as oxalate cannot be collected. Plasma oxalate measurements should be obtained in patients with unexplained kidney disease. 1,14

For more information on PH1, visit Alnylam.com

PH1 Facts

- PH1 is ultra-rare—1-3 per million people diagnosed in North America and the EU
- PH1 primarily presents in childhood
- PH1 is usually diagnosed during early childhood
- Majority of people living with PH1 present with kidney stones
- Kidney stones can result in:
  - Flank pain
  - Urinary tract infections
  - Painful urination
  - Blood in the urine
  - Surgery for removal

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