Primary Hyperoxaluria Type 1 Backgrounder

Disease Overview

Primary hyperoxaluria (PH) constitutes a group of rare inherited disorders of the liver characterized by the overproduction of oxalate, an end-product of metabolism. High levels of oxalate are toxic because oxalate cannot be broken down by the human body and accumulates in the kidneys.[1,2]

There are 3 types of PH: type 1 (PH1), type 2 (PH2), and type 3 (PH3). PH1 is the most common and severe form, accounting for 70% to 80% of all cases. PH1 affects 1 to 3 individuals per million, with a higher prevalence in some regions, such as the Middle East and North Africa.[1,3] In the United States and Europe, there may be approximately 2,500 to 5,000 cases.[4*]

Symptoms

People with PH1 often experience the formation of oxalate stones throughout the urinary tract and kidneys. When a person with PH1 has a kidney stone, symptoms can include flank pain, urinary tract infections, painful urination, and blood in the urine.[5]

PH1 Manifestations by Stage of Life	
Infancy	**Childhood/Adolescence/Adulthood**
Insufficient weight gain	Multiple kidney stones
Formation of kidney stones	Progressive kidney disease (including kidney failure)
Early end-stage renal failure	Multi-organ dysfunction

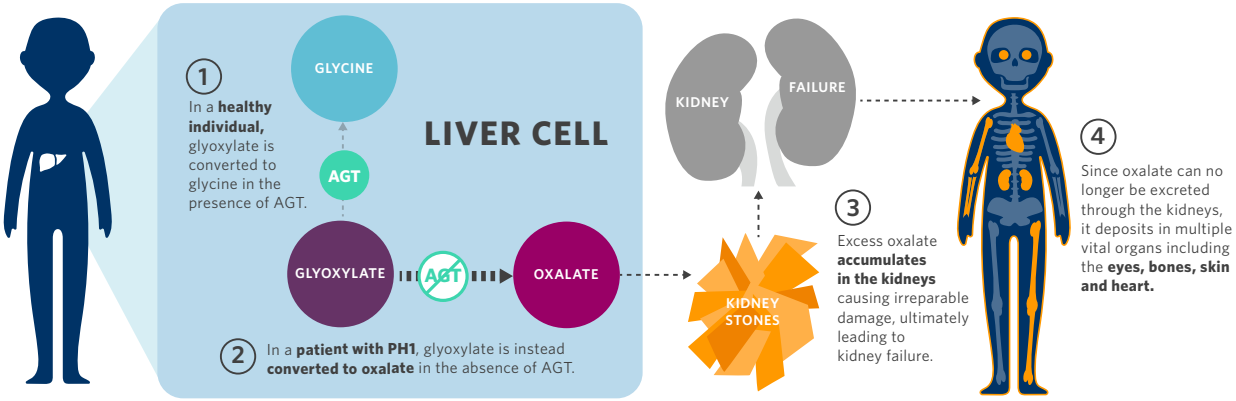
Over time, kidney function declines so that the kidneys can no longer excrete as much oxalate as they receive. This can often result in end-stage renal disease, a life-threatening condition that prevents the kidneys from filtering fluids and waste from the body effectively. As a result, oxalate levels in the blood rise and it begins to accumulate and deposit in the eyes, bones, skin, heart, and central nervous system, causing diminished vision, bone fractures, ulcers, heart failure, and other complications.[5]

Diagnosis

Patients can be diagnosed with PH1 at any age, but most individuals experience their first symptoms in early childhood. For many patients, PH1 is not diagnosed immediately. Since kidney stones in adults are more commonplace, adult patients with PH1 often spend many years undiagnosed until they present with severe kidney disease. Some individuals are not diagnosed until after their kidneys have failed and they require dialysis to help filter waste products from the blood.[5]

Cause

PH1 is caused by a genetic defect in a liver enzyme called alanine-glyoxylate aminotransferase, or AGT.[1] 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, initially in the kidneys, and, when the disease advances, in other vital organs of the body.



Treatment

For patients with advanced disease, the only curative treatment is a liver transplant, to correct the metabolic defect, combined with a kidney transplant, to replace the terminally damaged kidneys.[1,2]

For more information on primary hyperoxaluria type 1 visit Alnylam.com/patients/primary-hyperoxaluria or contact media@alnylam.com.

*These estimates assume an approximately 50% diagnosis rate based on the publication by Hopp et al.[4]

1. Cochat P and Rumsby G. Primary hyperoxaluria. *N Engl J Med*. 2013;369:649-658 .
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5. Milliner DS et al. *GeneReviews®*; [updated Nov 30, 2017]. https://www.ncbi.nlm.nih.gov/books/NBK1283/.