Cystinuria

Cystinuria is an autosomal recessive disease caused by a defect of an amino acid transporter in the proximal tubule of kidneys. This defect prevents proper reabsorption of basic, or positively charged amino acids, including cystine, ornithine, lysine and arginine. Inability to reabsorb these amino acids causes them to become concentrated in the urine. Cystine is a dimer formed by a sulfide bond between two cysteine amino acids. Accumulation of cystine in the urine can precipitate out, resulting in kidney stones. Cystine crystals form hexagonal-shaped crystals, and can be seen under microscopic analysis of the urine. These crystals can enlarge to form staghorn kidney stones as well. If not treated properly, the disease can cause serious damage to the kidneys. Stones can be identified by a positive nitroprusside test. Initial treatment is adequate hydration and alkalization of the urine with acetazolamide, because the cystine stones are more likely to precipitate in acidic urine. However, once large renal stones have formed, surgery may be required to remove them.

PLAY PICMONIC

Pathophysiology

Defect of Renal Tubular Amino Acid Transporter

Kidney-tuba with Amigo Acidic-lemon Transporter

The main pathophysiologic mechanism behind cystinuria is a defective amino acid transporter in the proximal tubule of nephrons in the kidney. These defective proteins are due to genetic mutations in the *SLC3A1* and/or *SLC7A9* genes. As a consequence, appropriate reabsorption of basic or positively charged amino acids is prevented.

C-O-L-A Acronym

Cola

COLA is an acronym for the amino acids that are unable to be reabsorbed in this disease: (dibasic) cysteine, ornithine, lysine, and arginine.

Cystine

Sistine (Chapel)

Cystine is not technically an amino acid. It is a dimer of cysteine amino acids. In this dibasic form, cystine is unable to be reabsorbed and thus may precipitate in the urine as cystine stones.

Ornithine

Hornet

Ornithine is also technically not an amino acid. However, it is an important molecule for biochemical pathways in the body, including the urea cycle. Ornithine is not reabsorbed in the proximal tubule of the kidney in cystinuria.

Lysine

L-icing

Lysine is a basic amino acid that is not reabsorbed due to the defect in the kidney transporter.

Arginine

Argentina-flag

Arginine is a basic amino acid that is not reabsorbed due to the defect in the kidney transporter.

Signs and Symptoms

Excess Cystine in Urine

Crystals in Urine

Cystine can precipitate out of urine and form kidney stones (nephrolithiasis).

Hexagonal Crystals

Hexagonal Crystal

Microscopically, cystine precipitates as hexagonal crystals. A urinalysis can be performed to look for these crystals and aid in diagnosis.

Staghorn Kidney Stones

Stag with Staghorn Kidney Stones

Staghorn kidney stones are upper urinary tract stones that involve the renal pelvis and extend into at least two of the calyces. All types of urinary stones can potentially form staghorn calculi, but the majority are composed of struvite-carbonate-apatite matrix. Patients with cystinuria can form staghorn calculi due to extensive precipitation of cystine out of the urine.

Diagnosis

Cyanide Nitroprusside Test

Sai Nitro-puss

The cyanide nitroprusside test is a urinalysis test used to identify cystine present in the urine. In this test, cyanide nitroprusside is added to urine and left alone for approximately 10 minutes. In this time, disulfide bonds within cystine molecules will be broken by the cyanide, releasing cysteine amino acids and changing the urine to a purple color. Therefore a color change indicates the presence of urinary cystine.

Treatment

Acetazolamide to Alkalinize the Urine

A-cheetah-Zorro with Up-arrow pH-strip

Acidic urine favors cystine precipitation; therefore, treatment with acetazolamide, a diuretic that alkalinizes urine, can be used to help prevent stone formation in cystinuria.