Ornithine Transcarbamylase Deficiency

Ornithine transcarbamylase deficiency is a metabolic disorder caused by a deficiency of the enzyme ornithine transcarbamylase. This enzyme catalyzes the reaction between carbamoyl phosphate and ornithine to form citrulline, which is a key step in the urea cycle. Because the enzyme deficiency causes a defect in the urea cycle, the body's ability to get rid of ammonia is affected and patients exhibit hyperammonemia. An ornithine transcarbamylase deficiency is often evident in the first few days of life, with failure to thrive as the most commonly seen symptom. Some babies may experience seizures or even coma, and complications may include developmental delay and mental retardation. Another symptom of this enzyme deficiency is the buildup of orotic acid in the blood, as the substrate carbamoyl phosphate enters the pyrimidine synthesis pathway and forms orotic acid. The buildup of orotic acid can often be confused with orotic aciduria, caused by a deficiency in a bifunctional protein that includes the activities of orotate phosphoribosyltransferase and orotidine 5' – phosphate decarboxylase in the pyrimidine synthesis pathway. The hereditary form of orotic aciduria can be distinguished from an increase in orotic acid secondary to an ornithine transcarbamylase deficiency by evaluating blood ammonia levels. In a urea cycle deficit caused by a defect in ornithine transcarbamylase, there will be hyperammonemia and decreased BUN. Ammonia levels are within normal limits in the hereditary form of orotic aciduria. Ornithine transcarbamylase deficiency is the most common urea cycle disorder, and unlike the majority of metabolic enzyme deficiencies, ornithine transcarbamylase is inherited in an X-linked recessive fashion.

PLAY PICMONIC

Pathophysiology

Most Common Urea Cycle Disorder

#1 Foam-finger U-rainbow Cycle

Ornithine transcarbamylase deficiency is the most common urea cycle disorder.

X-Linked Recessive

X-suit with Recessive-chocolate

Unlike the majority of metabolic enzyme deficiencies, ornithine transcarbamylase deficiency is inherited in an X-linked recessive fashion. This means that this disorder is more prevalent in males than females.

Signs and Symptoms

Hyperammonemia

Hiker-ammo

Because this enzyme deficiency causes a defect in the urea cycle, the body's ability to get rid of ammonia is affected, and patients exhibit hyperammonemia. An important note regarding hyperammonemia in this disease is that the prognosis of the disease is correlated to the length of exposure to high ammonia levels rather than the level of ammonia. Thus, those who have been exposed to hyperammonemia for extended periods often have a worse clinical picture than those who may have had a very high level of ammonium for a short amount of time.

Decreased BUN

Down-arrow Hot-dog-BUN

The buildup of orotic acid in ornithine transcarbamylase can often be confused with orotic aciduria, a disorder caused by a deficiency in a bifunctional protein that includes the activities of orotate phosphoribosyltransferase and orotidine 5' – phosphate decarboxylase in the pyrimidine synthesis pathway. The hereditary form of orotic aciduria can be distinguished from an increase in orotic acid secondary to an ornithine transcarbamylase deficiency by evaluating blood ammonia levels. In a urea cycle deficit caused by a defect in ornithine transcarbamylase, there will be hyperammonemia and decreased BUN.

Carbamoyl Phosphate is Converted to Orotic Acid

Car-bomb-oil with Phosphate-Ps Converting to Erotic Acidic-lemons

Another result of this enzyme deficiency is the buildup of orotic acid in the blood. This buildup occurs as the substrate carbamoyl phosphate enters the pyrimidine synthesis pathway and forms orotic acid.

Pyrimidine Synthesis Pathway

Pyramid

In this disorder, the deficiency of the enzyme ornithine transcarbamylase leads to an excess buildup of carbamoyl phosphate. As excess carbamoyl phosphate enters the pyrimidine synthesis pathway, it is converted to orotic acid, leading to an abnormal increase of orotic acid in the blood and urine.

Evident in Babies

Baby

This deficiency is often evident in the first few days of life with failure to thrive. Other early findings of ornithine transcarbamylase deficiency include irritability, vomiting, excessive somnolence, and uncontrolled body movements.