Orotic Aciduria

Orotic aciduria is an autosomal recessive metabolic disorder characterized by excessive excretion of orotic acid in the urine. The genetic disorder is caused by a deficiency in a bifunctional protein that includes the activities of orotate phosphoribosyltransferase and orotidine 5’ – phosphate decarboxylase, which is an enzyme in the de novo pyrimidine synthesis pathway. In additional to excessive orotic acid in the urine, patients typically have a megaloblastic anemia which cannot be cured by administration of vitamin B12 or folate. Orotic aciduria can also lead to inhibition of RNA and DNA synthesis and failure to thrive. Treatment includes oral uridine administration, which can reduce the urinary orotic acid and anemia. Excess orotic acid in the urine can also be caused by a blockage of the urea cycle, especially ornithine transcarbamylase deficiency. The hereditary form 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, there will be hyperammonemia and a decreased BUN. However, ammonia levels are within normal limits in the hereditary form of orotic aciduria.



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Pathophysiology

Autosomal Recessive
Recessive-chocolate
This disease is inherited in an autosomal recessive fashion.

Defect in UMP Synthase
Broken UMP
The enzyme UMP synthase plays a role in the conversion of orotic acid to uridine monophosphate (UMP). The defect in this enzyme causes an inability to convert orotic acid to UMP.

De Novo Pyrimidine Synthesis Pathway
Pyramid Pathway
Patients with orotic aciduria have a deficiency of UMP synthase. This enzyme is important in the de novo pyrimidine synthesis pathway.

Symptoms

Increased Orotic Acid in Urine
Up-arrow Erotic Acidic-lemons in Urine-from-urinal
The defect in the enzymes orotic acid phosphoribosyltransferase and orotidine 5'-phosphate decarboxylase causes a buildup of orotic acid in the body. Excess orotic acid in the urine can also be caused by a blockage of the urea cycle, especially ornithine transcarbamylase deficiency. The hereditary form can be distinguished from an increase in orotic acid secondary to an ornithine transcarbamylase deficiency by evaluating blood ammonia levels.

Megaloblastic Anemia
Mega-blast Anemone
Patients typically have megaloblastic anemia, which cannot be cured with the administration of vitamin B12 or folate.

No Response to B12 or Folate
No Effect from (12) Dozen Viking Bees and Foliage
In orotic aciduria, patients develop megaloblastic anemia, which is refractory to vitamin B12 or folic acid administration.

Non-Hyperammonemic
Nun-hiker-ammo
Excess orotic acid in the urine can also be caused by a blockage of the urea cycle, especially ornithine transcarbamylase deficiency. The hereditary form 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, there will be hyperammonemia and a decreased BUN. Ammonia levels are within normal limits in the hereditary form of orotic aciduria.

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Failure to Thrive

Very Skinny Baby

Orotic aciduria can also lead to the inhibition of RNA and DNA synthesis and failure to thrive.

Treatment

Oral Uridine Monophosphate

Udon-noodles

The administration of oral uridine is converted to uridine monophosphate (UMP) and bypasses the metabolic block created by the enzyme deficiency.

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