AMINO ACID DISORDERS

Phenylketonuria
6-PTPS Deficiency

What is 6-PTPS Deficiency?

Phenylalanine hydroxylase requires BH4 for activity in the hydroxylation to tyrosine.[3] A deficiency of BH4 can result in increased phenylalnine levels in the blood. It is important to note that BH4 is also a co-factor of the enzymes tyrosine and tryptophan hydroxylase.[1]

CLINICAL MANIFESTATIONS

Patients are normal at birth but some may present with early hypotonia; developmental delay may be apparent by the 2nd to 3rd month presenting with seizures and leading to a progressive neurological degenerative disease.[3]

PATHOPHYSIOLOGY

The lack of the cofactor causes increases of phenylalanine in the blood and other tissues. Similar to phenylketonuria, elevated phenylalanine interfere with myelination, synaptic sprouting and dendritic pruning.[4]

Inheritance: autosomal recessive[1,3]

CONFIRMATORY TESTING

Plasma amino acids, urine proteins, DHPR enzyme assay. Further confirmatory testing (i.e. BH4 loading) may be required after referral to a metabolic specialist.

Overview of Disease Management

Patients with defects in pterin metabolism, especially with abnormalities of BH4 synthesis should be treated with BH4 with a daily dose of 2-Smg/kg.[3] Patients are also supplemented with levodopa {8-12 mg/kg/day) and 5-OH Tryptophan (6-9mg/kg/ day)[5] Initiation of management should be done in consultation with an attending physician/metabolic specialist.

Prognosis

When treatment is started early, motor and intellectual development can be normal.[3]

*Patients with 6-PTPS deficiency are not prone to metabolic crisis. Medications are to be maintained when they are sick.
*If there are queries about the management, contact the metabolic doctor on call.

However, for the enzyme to function properly, it needs the support of a co-factor. In this case, the co-factor is known as tetrahydrobiopterin or BH4. BH4 in turn is produced by our body through a series of metabolic processes which also makes use of enzymes. A lack of the 6-PTPS enzyme causes a decrease in the production of BH4 which in turn affects the breakdown of phenylalanine.

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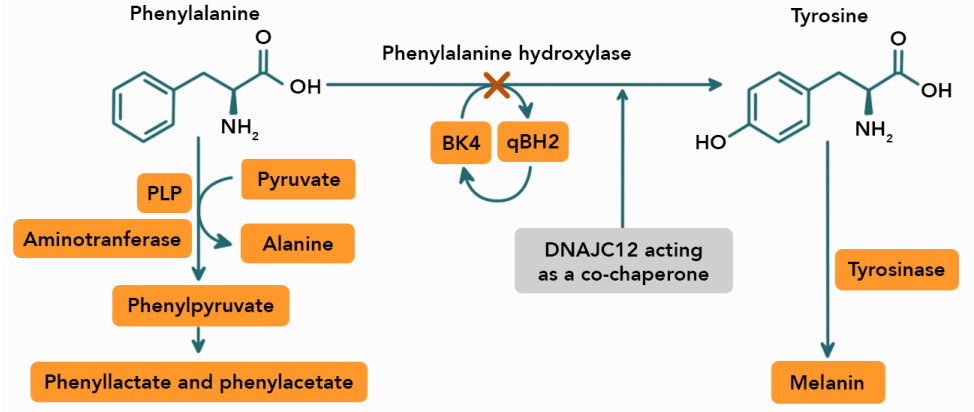
6-PTPS patient's breakdown of protein:



What are the signs and symptoms of untreated 6-PTPS deficiency?

Children are normal at birth although some may present with decreased muscle tone. At about 2-3 months of age, they may present with seizures and developmental delay which can progress.

What is the treatment of 6-PTPS deficiency?

Dietary control is not needed. Supplementation with BH4, levodopa and 5-0H tryptophan should be given daily in divided doses.

What should I do when my baby is sick?

The medications should be continued and consult with a doctor as needed should be done.

[3] *Nyhan WI., Barshop BA and AI-Aqeel A. Chapter 16: Hyperphenylalaninemia and defective metabolism of tetrahydrobiopterin. Atlas of inherited Metabolic Diseases 3rded. Great Britain:Oxford University Press, 2012 pp123-135*
[4] *Kaye Cl and the CommiOee on Gene cs. Newborn screening fact sheets. Pediatrics 2006;118:934-963*
[5] *Zchocke J and Hoffmann GF, Vademecum Metabolicu, 3rd ed., Germany:Milupa Metabolics, 2011*