A Case With High Phenylalanine Level Mimicking Classical Phenylketonuria: PTPS Deficiency

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6-Pyruvoyl-Tetrahydropterin Synthase (PTPS) Deficiency is the most common cause of BH⁴ deficiency. Affected infants may present with neurological deterioration like truncal hypotonia, increased limb tone, bradykinesia, episodic rigidity and oculogyric crisis.(1) Herein a PTPS deficiency who presents with a high level of phenylalanine in newborn screening was presented.

The patient was the third living child of a consanguineous parent born at 36th gestational age, 2000 gr small for gestational age. She was referred for hyperphenylalaninemia detected on newborn screening and her plasma phenylalanine level was 2460 μmol/L suggesting as classic phenylketonuria. Phenylalanine levels were in normal range with dietary phenylalanine restriction but she did not admit to the hospital for her routine control until 8 months of age. At 8 months of age, she had truncal hypotonia, hypertonicity on her lower limbs and she had no eye contact. Pterin analysis in dried blood samples was performed and revealed high neopterin (3.39 nmol/g Hg, reference range 0.19-2.93) and low biopterin (0.01 nmol/g Hg, reference range 0.08-1.20) level which were indicative for PTPS deficiency. Combined treatment with BH⁴, L-dopa with carbidopa and folinic acid, then 5-Hydroxytryptophan started. Her dietary protein tolerance significantly increased. A homozygote mutation on PTB gene (p. Thr67Met) detected with molecular analysis confirmed the diagnosis.

Pyruvoyl-tetrahydropterin synthase (PTPS) deficiency is the most common disorder among causes of BH⁴ deficiency. Phenylalanine levels may be within normal range or detected slightly upper normal or prominently higher, therefore patients may be misdiagnosed as classical PKU. In many cohorts of subjects with PTPS deficiency FA levels are below 2400 μmol/L.(2-5) Despite these findings rarely in PTPS deficiency FA levels can exceed 2400 μmol/L as classical PKU. Similarly in a study 4 of 22 PTPS deficient patients had phenylalanine levels above 2400 μmol/L.(6) In conclusion it should be noted that HFA is not only caused by PKU deficiency. All HFA patients and infants with typical neurological findings should be screened for BH⁴ deficiency.

2. Thony B, Auerbach G, Blau N. Tetrahydrobiopterin biosynthesis, regeneration