Case Report

A Case Report: Phenylketonuria in a one-year-old child from India

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International Archives of Integrated Medicine, Vol. 4, Issue 9, September, 2017.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 07-08-2017 **Accepted on:** 12-08-2017
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Punam Kumari Jha, Nalin Chaudhary, Abhinav P. A Case Report: Phenylketonuria in a one-year-old child from India. IAIM, 2017; 4(9): 187-190.

Abstract

Phenylketonuria is a rare genetic disorder caused by an inborn error in aromatic amino-acid metabolism resulting a lack of mental abilities and developmental changes. Phenylketonuria is an autosomal-recessive inherited metabolic disease in which excessive accumulation of phenylalanine occurs which further leads to neurological impairment. In this paper we report a case of a one-year-old child born with the consanguineous parent with distinct amino acid analysis and radiological findings.

Key words

Phenylketonuria, Child, India.

Introduction

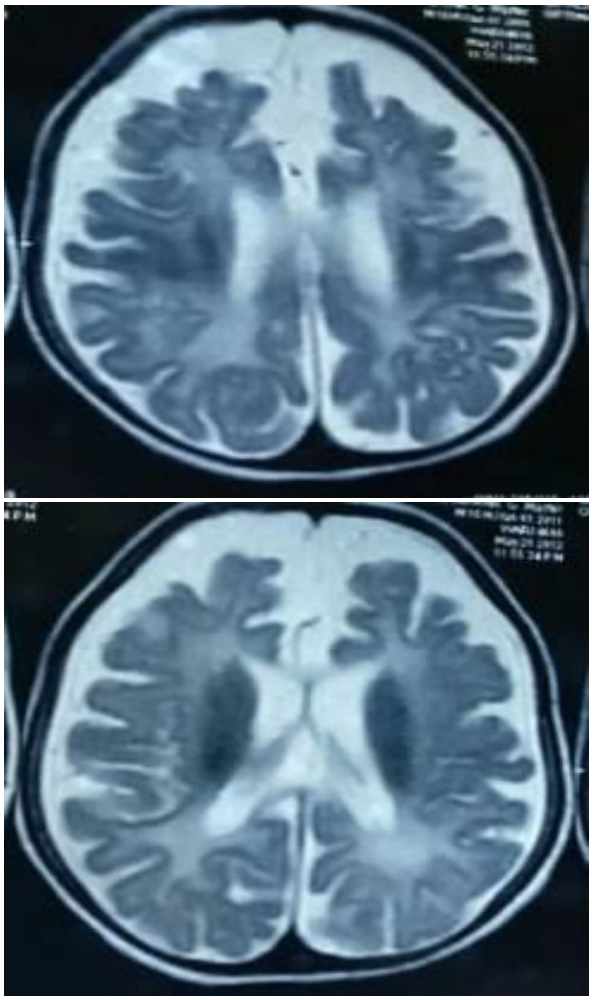
Phenylketonuria (PKU) is an inborn error of protein metabolism caused predominantly by mutations that result from an impaired ability to metabolize the essential amino acid phenylalanine. PKU is an autosomal-recessive inherited metabolic disease in which mutations in phenylalanine hydroxylase (PAH) gene or the gene encoding its cofactor, tetrahydrobiopterin (BH4) results in decreased catabolic pathway of phenylalanine. The lack of PAH or its cofactor BH4 which results in the accumulation of excess phenylalanine, that impairs intellectual abilities if untreated. The classic PAH deficiency is considered when the serum concentration of unchanged phenylalanine (Phe) crosses the level of 1200-µmol/L. The Phe concentration in the

range of 600 to 1200-µmol/L is diagnosed as mild PKU, and values less than 600-µmol/L are classified as hyperphenylalaninemia (HPA).When the treatment program of a patient with PKU did not start at the early weeks of neo-natal period developmental delay, mental retardation and microcephaly are caused by the accumulation of toxic byproducts of Phe within its metabolic pathway [1].

Case report

A one-year-old male child was born to consanguineous parent by NVD. The child cried after birth and weighs 3.5kgs. On examination the child was alert and no proper eye to eye contact, fontanelle closed, brachy/microcephaly, mild spasticity in lower limbs and moving all limbs, no facial asymmetry, plantar reflux is raised. Radiological data presents with cerebral atrophy, bilateral diffuse white matter changes in MRI scan (**Figure - 1, 2**). Provisional diagnosis to be Metachromatic Leukodystrophy (MLD)/ Aminoaciduria/ Leigh syndrome. He had been advised for Urine and serum aminoacid test, thyroid hormone stimulating test, creatinine phosphor- kinase(CPK), nerve conduction study(NCS), serum lactate pyruvate tests. He had kept on physiotherapy and on anti-epileptic medications. Later when the child visited for the outpatient department with conditions of global developmental delay, right focal seizures, poor visual perception and not yet attained social smile, head control, rolling eyes during the 2nd month after birth. On examination weight 7 kg, hypopigmented scalp hair, increased tone, deep tendon reflux (DTR) scoring 5.MRI-brain suggests of severe global developmental delay/microcephaly/seizure disorder. He had screened for plasma aminoacid analysis and the method used was reverse phase HPLC. The treatment continued as same. The diagnosis was confirmed by elevated levels of phenylalanine levels 300 µmol/L (31-75 µmol/L), urine metabolic screening reports are positive for ferric chloride test. He is recommended for Phenylalanine restricted diet to be initiated and kept on regular anti-seizure medications and recommended for physiotherapy.

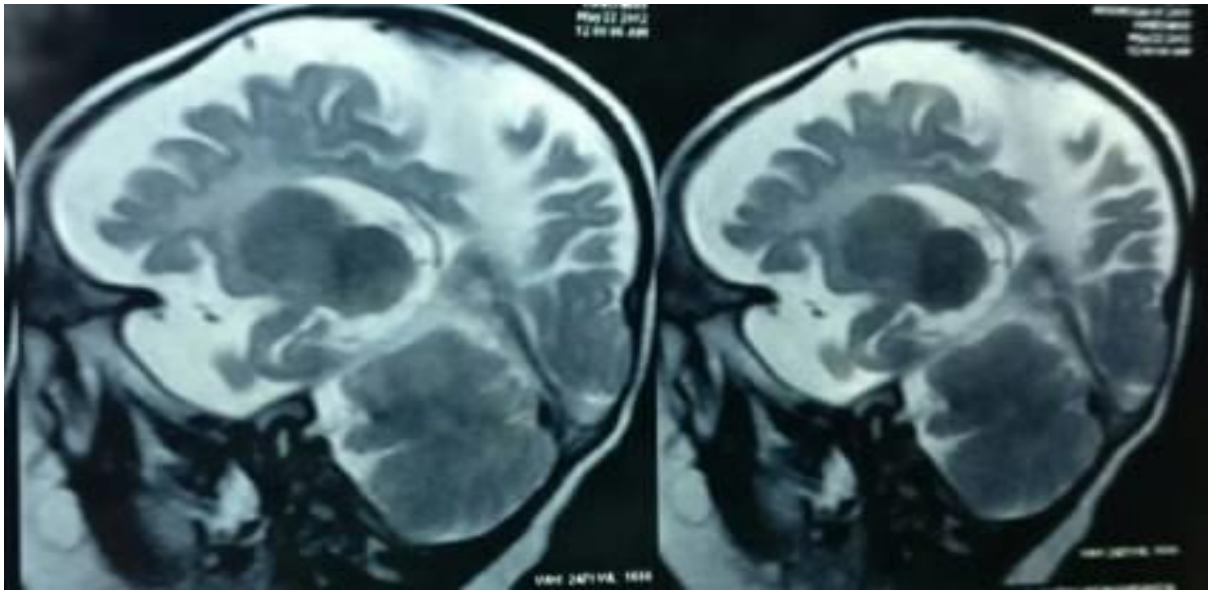
Figure – 1: Diffuse bilateral white matter changes seen in MRI of the patient.



Discussion

Dr. Fölling had discovered that phenyl pyruvic acid which is responsible for the disturbance in the metabolism of the aminoacid during 1934 called phenylalanine which was subsequently named as “phenylketonuria” later developed by Penrose a Quastel. Jervis in 1953 identified the metabolic error and Bickel, et al. [3] in 1954 reported the success of low phenylalanine diet therapy [2]. The incidence of PKU or HPA is highest amongst Caucasians, occurring in approximately 1 in 10,000 births [3]. The prevalence of PKU varies by country ranging from between one in 10,000 and one in 20,000 births in U.S.A. and Europe [4].

Figure – 2: Cerebral atrophy changes in the patient MRI.



The error in the genetic information affects the metabolism of the protein module phenylalanine, an essential amino acid, which is normally in the liver turned into the amino acid tyrosine. In the process of biosynthesis the "wrong" amino acid is assembled, as a result of the mutation. This leads to a missing or lacking activity of the enzyme which turns phenylalanine into tyrosine. The surplus of phenylalanine accumulates in blood and tissues and causes a brain damage [5]. In this case, there is impairment in both the mental and neurological development is seen at early stages.

The natural history of the phenylketonuria consists in a progressive irreversible neurological impairment during infancy and childhood. The most common outcome is severe mental retardation often associated with a "mousy" odor, eczema and reduced hair skin and iris pigmentation; also reduced growth, microcephaly and neurological signs as tremor, epilepsy are present.

All untreated patients have behavioral problems as hyperactivity, stereotypy and anxiety. The severity of the clinical phenotype directly correlates with blood phenylalanine levels that reflect the degree of enzymatic deficiency [6]. The urine samples were tested for a number of substances including ketones. When ketones are present, urine usually develops a red-brown color upon the addition of ferric chloride, but in this instance the urine yielded a dark-green color [7].

The PKU suggests that the metabolic abnormalities could cause neurological effects and also shows the importance to treat these abnormalities and that will lead to positive clinical outcomes. The development of Guthrie's screening test, and dietary treatment led to the prevention of intellectual impairment in affected children throughout the world. Furthermore, the PKU model has since been used as a template to shed light on over 200 other inborn errors of metabolism [8, 9].

Patients with PKU should still be treated with dietary therapy, but in the long term the introduction of a wide array of new treatment approaches such as more palatable foods based on the use of GMP products or the administration of LNAA or BH4 could decrease the need for phenylalanine restriction in the diet. Patients' surveys show that GMP foods have improved taste and are preferred a standard formula [6]. The foundation of PKU treatment is a low Phe diet which, by reducing or normalizing Phe concentrations, prevents the development of the neurological and psychological changes. Since

neurological changes have been demonstrated within one month of birth, it is recommended that dietary restriction should be started early and be continued through childhood when neural development is maximal [10].

Conclusion

PKU is an autosomal recessive inborn error. Due to which an impaired ability to metabolize the essential amino acid phenylalanine occurs that may cause the disease. PKU have been discovered over 70 years ago and the correlation between the metabolic and neurological development lead to neonatal screening and appropriate treatment leads to positive clinical outcomes. Long-term dietary requirements, physical activity, growth and intellectual skills need to be monitored in patients with PKU.

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