Nutrition 59 (2019) 180–181

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Case study

Transient phenylketonuria in premature infants

Beatriz Salamanca-Zarzuela Pediatricians [a,*], María Elena Infante López Pediatricians [b], Carlos Alcalde Martín Pediatricians [a]

[a] Department of Pediatrics, Hospital Universitario Rio Hortega, Valladolid, Spain
[b] Department of Neonathology, Hospital Universitario Rio Hortega, Valladolid, Spain

ARTICLE INFO

Article History:
Received 21 March 2018
Accepted 11 August 2018

ABSTRACT

Phenylketonuria (PKU) is an autosomal recessive inborn error of phenylalanine (phe) metabolism caused by a deficiency in the enzyme phenylalanine hydroxylase that converts phe into tyrosine. If left untreated, PKU results in increased phe concentrations in the blood and in the brain, which cause severe intellectual disability, epilepsy, and behavioral problems. These disorders can be prevented if a diet low in phe is introduced. This report focuses on a preterm newborn (gestational age 29 wk) with adequate weight (1290 g) and no family history of PKU. His parents had not received metabolic neonatal screening. A blood sample at 16 d of age and a weight of 1430 g showed phe 420 μmol/L, compatible with mild PKU. Mixed feeding was initiated with a formula free of phe (X-Phe), and breastfeeding was fortified with a contribution of 3.5 g/kg daily (2.5 g X-Phe and 1 g of high-value biological proteins). The next measurements of amino acid levels in the blood and urine were normal, and the progenitors study for PKU was negative. Normal feeding was reintroduced with normal neurologic and metabolic later evolution. The disorders of the metabolism of phe, in most cases, are due to a genetic condition. However, there are infrequent cases of transient hyperphenylalaninemia secondary to delayed maturation of the hydroxylation enzyme system. They are especially significant in premature infants. Although these forms have not been shown to cause sequelae, in view of high levels of phe in the blood, phe consumption must be restricted.

Phenylketonuria (PKU) is the most frequently occurring hereditary metabolic disorder. Its frequency ranges from 1 in 4000 to 40 000 live births. PKU is an autosomal recessive inborn error of phenylalanine (phe) metabolism caused by a deficiency in the enzyme phenylalanine hydroxylase, that converts phe, together with its cofactor tetrahydrobiopterin (BH4), into tyrosine. If left untreated, PKU results in increased phe concentrations in the blood and in the brain, which cause severe intellectual disability, epilepsy, and behavioral problems. These disorders can be prevented if a diet low in phe is introduced. To be useful, this dietary treatment must begin in the first days of life and before clinical symptoms appear. Screening programs in newborns and early dietary treatment have drastically modified the prognosis [1,2].

For neonatal screening, a capillary blood sample obtained by puncturing the heel of the newborn is usually obtained by impregnating an absorbent paper with a standardized volume. The Commission of Congenital Metabolic Errors of the Society of Clinical Biochemistry and Molecular Pathology recommends that, as a general rule, the extraction of blood from the heel be carried out as soon as possible after 48 h of life, with protein feed established, either by enteral or parenteral nutrition [1].

Complete enzyme deficiency results in classic PKU, in which serum phe concentration are >20 mg/dL (1200 μmol/L). Residual enzyme activity causes moderate PKU (phe concentrations 900–1200 μmol/L), mild PKU (phe concentrations 600–900 μmol/L), mild hyperphenylalaninemia (HPA; phe concentrations 360–600 μmol/L), and benign mild HPA not requiring treatment (phe concentrations 120–360 μmol/L) [3,4].

We present the case of a preterm newborn (29 + 4 wk gestational age) with adequate weight for his gestational age (1290 g). In the immediate neonatal period, the newborn presented with distress that required noninvasive mode continuous positive airway pressure for 11 d, without other complications. There was no family history of PKU. The newborn's parents were foreign and had not received metabolic neonatal screening. They had an older, healthy female child. A blood sample was taken on blotting paper for metabolic screening. Enteral feeding was initiated with fortified breastfeeding, which included a daily protein intake of 3.5 g/kg. A new blood sample was taken on blotting paper at 16 d of age, weight 1430 g. At that time, results showed phe 420 μmol/L, which is compatible with mild PKU. The newborn was started on mixed feeding with a formula free of phe (X-Phe) and breastfeeding fortified with a daily contribution of 3.5 g/kg of free proteins (2.5 g X-Phe and 1 g of high-value biological proteins), assuring also the necessary caloric and volumetric contribution for a preterm

* Corresponding author: Tel.: +34 662 507052; Fax: +34 983 331566.
E-mail address: beatrizsalamanca@hotmail.com (B. Salamanca-Zarzuela).

https://doi.org/10.1016/j.nut.2018.08.013
0899-9007/

of the newborn's age and weight. The subsequent measurement of amino acid levels in the blood and urine were normal, and the progenitors study for PKU was negative. Normal feeding was reintroduced, with normal neurologic and metabolic later evolution.

In most cases, the disorders related to the metabolism of phe are due to a genetic condition, with autosomal recessive inheritance, by mutations in a gene located on chromosome 12 (12 q24.1), which encodes the enzyme phenylalanine hydroxylase [1,2].

However, there are infrequent cases of transient HPA secondary to delayed maturation of the hydroxylation enzyme system. In these cases, serum phe levels are higher than the upper limit of normal, but lower than those of classical PKU. The levels decrease with time and without causing symptoms [5]. Our patient presented especially high levels of phe for this type of PKU. These cases appear in patients heterozygous for the mutation, or in the context of generalized inflammatory processes secondary to drugs or renal failure. They are especially significant in the neonatal period, especially in premature infants, due to the functional immaturity of the enzymatic system of oxidation of the aromatic amino acid phe [6]. Although these forms have not been shown to cause sequelae, in view of high levels of phe in the blood, consumption of phe must be restricted. But Its necesary ensuring an adequate total protein intake, until ruling out a classic form of PKU, since there is a risk for neurologic involvement, especially in patients of such a young age.

References

[1] Matilde G, López C, Parrilla FJ, Martínez AL. Screening neonatal. Protocolos Diagnóstico Terapeúticos de la AEP: Neonatología 2008;1:423–33.
[2] Van Wegberg AMJ, Macdonald A, Ahring K, Blau N, Bosch AM, Burlina A. The complete European guidelines on phenylketonuria: diagnosis and treatment. Orphanet J Rare Dis 2017;12:162.
[3] Viall S, Ayyub O, Rasberry M, Lyons K, Ah Mew N. "Mild" hyperphenylalaninemia? A case series of seven treated patients following newborn screening. Mol Genet Metab 2017;122:153–5.
[4] Camp KM, Parisi MA, Acosta PB, Berry GT, Bilder DA, Blau N, et al. Phenylketonuria Scientific Review Conference: state of the science and future research needs. Mol Genet Metab 2014;112:87–122.
[5] Cristina P, Pinto G. Hiperfenilalaninemia transitória em recém-nascido prematuro: um relato de caso [Transient hyperphenylalaninemia in preterm newborns: a case report]. HU Revista 2010;36:251–4.
[6] Hennermann JB, Loui A, Weber A, Mönch E. Hyperphenylalaninemia in a premature infant with heterozygosity for phenylketonuria. J Perinat Med 2004;32:383–5.