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LETTER TO THE EDITOR

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NONGENETIC CAUSES OF HYPERTYROSINEMIA THAT MUST BE CONSIDERED WHEN INTERPRETING A FINDING OF ELEVATED URINARY TYROSINE

CAUSAS NO GENÉTICAS DE HIPERTIROSINEMIA QUE DEBEN CONSIDERARSE AL INTERPRETAR UN HALLAZGO DE TIROSINA ELEVADA EN ORINA

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LETTER TO THE EDITOR

Mr Editor:

In several countries newborns are screened for tyrosinemia type 1 using tyrosine as a primary marker [1]. In some situations elevated tyrosine levels in blood are discovered due to elevated tyrosine in a metabolic urine screening[2]. In Peru, some pediatric patients suspected of having a genetic condition (inborn error of metabolism) undergo a metabolic urine screening that includes - among other things - qualitative detection of tyrosine. However, when there are elevated levels of tyrosine in urine this does not always mean that the patient has a genetic condition[2,3]. Most often hypertyrosinemia has a non-genetic origin[2]. Therefore, it is important to review the non-genetic causes of hypertyrosinemia and thus avoid potential misinterpretations of this finding.

The genetic entities associated with increased levels of tyrosine are those that generate an enzymatic deficiency in the degradation of tyrosine, within which tyrosinemias type I, II or III are included [2,3]. However, elevated tyrosine levels in the blood usually have a nongenetic cause [2]. The most common non-genetic cause of increased tyrosine levels in the blood is transient tyrosinemia of the newborn [2]. This is due to immaturity of enzymes involved in tyrosine degradation [2,3]. – such as 4-hydroxyphenylpyruvate dioxygenase [4]. – such as 4-hydroxyphenylpyruvate dioxygenase [4].

It should be noted that two full-term infants have been reported to have received high-protein diets (3 to 4 times more than recommended), so the tyrosine concentration was > 10 times normal [5]. Plasma tyrosine quickly returned to normal after switching to an appropriate formula [5]. Therefore, even in full-term infants, a diet high in protein is a risk factor for transient tyrosinemia in the newborn [5]. In fact, some authors point out that in general, hypertyrosinemia could be caused by a diet with sufficiently high levels of proteins [3] and by vitamin C deficiency [2,4].

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Transient tyrosinemia of the newborn resolves spontaneously and no significant negative effects are generally observed, even more so if hypertyrosinemia has been maintained only for a short period[4,5]. However, mild developmental delay [4] and learning disabilities have been reported after 9 years of follow-up, especially in those with very high tyrosine levels (>1100 umol/L)[5], as increased levels of tyrosine in the blood apparently do not cause disease if they are < 500 uM[2].

Although the resolution is spontaneous, it should be noted that there is a rapid response to pharmacological doses of vitamin C [2]. Liver dysfunction or failure of any cause can lead to elevated tyrosine in the blood and increased excretion of tyrosine metabolites in urine [2-4]. LTyrosine levels in these cases are usually < 500 uM [2]. Because the latter is also observed in hereditary tyrosinemia type 1 (fumaryl acetoacetate hydrolase deficiency), in cases of liver damage the measurement of plasma alpha-fetoprotein and urine succinyacetone is important to define the cause [2].

Hypertyrosinemia may also occur in other situations, such as a blood sample without previous fasting (postprandial sample)[2,4], hyperthyroidism [2,4] and NTBC (2-(2-nitro-4-trifluoromethylbenzoyl)-1, 3-cyclohexanedione) therapy [2]. Therefore, there are non-genetic causes of hypertyrosinemia that must be considered to avoid false positives.

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