

A 9-Month-Old Boy with Seizures and Discrepant Urine Tryptophan Concentrations

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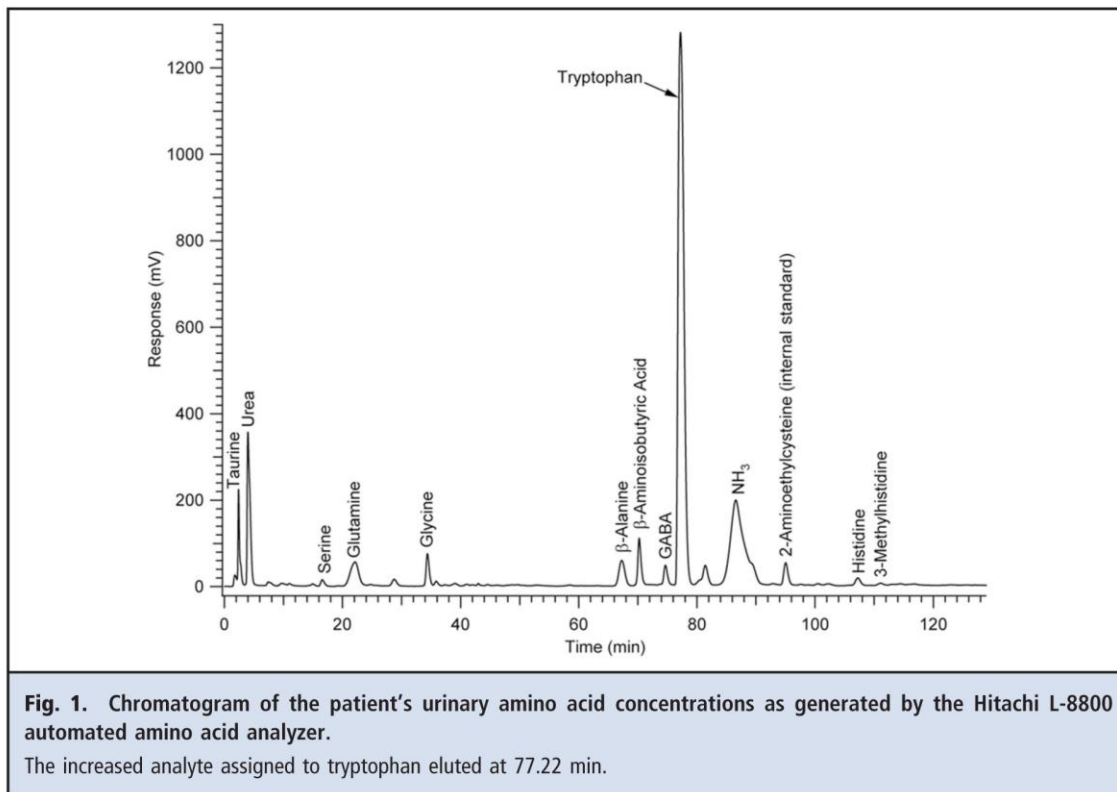
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CASE

A 9-month-old boy with a history of seizures underwent a neurologic and biochemical-genetic evaluation. The brain MRI results were compatible with a diagnosis of Leigh disease, also known as subacute necrotizing encephalomyelopathy, a rare neurometabolic disorder that affects the central nervous system. The patient had been prescribed several antiepileptic medications, including levetiracetam, lamotrigine, phenobarbital, vigabatrin, and topiramate. Metabolic screening for free amino acids was performed on the child's urine, with concentrations quantified with an automated amino acid analyzer (Hitachi L-8800). This commercially available system couples ion-exchange liquid chromatography with postcolumn ninhydrin derivatization before UV detection. This analysis revealed a very large peak with a retention time consistent with the elution of tryptophan (Fig. 1). The calculated urinary excretion was 125 204 $\mu\text{mol/g}$ creatinine. In addition, the urinary concentrations of γ -aminobutyric acid, β -alanine, β -aminoisobutyric acid, and glutamine were also increased substantially. The concentrations of the remaining amino acids were within their respective reference intervals. For confirmation, we submitted a urine aliquot to an external reference laboratory for analysis by liquid chromatography–tandem mass spectrometry. This analysis revealed a tryptophan excretion of 71 $\mu\text{mol/g}$ creatinine (reference interval, 15–302 $\mu\text{mol/g}$ creatinine).

Questions to Consider

- What are 2 pathologic conditions that produce large increases in urine tryptophan?
- What could potentially induce false increases in tryptophan concentrations when urine amino acids are quantified by ion-exchange liquid chromatographic separation and postcolumn ninhydrin derivatization before detection?
- On the basis their respective chemical structures, do any of the prescribed antiepileptic drugs (AEDs) react with ninhydrin and thus interfere with tryptophan measurement?



Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the April 2011 issue of *Clinical Chemistry*. To view the case and comments online, go to <http://www.clinchem.org/content/vol57/issue4> and follow the link to the Clinical Case Study and Commentaries.

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