A Four-Day-Old Boy with an Abnormal Metabolic Screen

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CASE DESCRIPTION

A four-day-old boy with a positive result in newborn-screening testing was referred to the hospital for further evaluation. He was the product of a 39-week gestation and appeared well at birth. His laboratory results included the following plasma findings: ammonia, 109 μg/dL (reference interval, 20–65 μg/dL); citrulline, 169 μmol/L (reference interval, 2–50 μmol/L); and leucine, 278 μmol/L (reference interval, 32–153 μmol/L). Also found were increases in homocysteine and γ-aminobutyric acid. The amino acid spectrum is shown below (Fig. 1).

QUESTIONS

1. What class of genetic disorders did this patient most likely have?
2. What enzyme deficiency was suggested by the patient’s amino acid profile, and how did you reach the conclusion?

The answers are on the next page.
Hyperammonemia is highly suggestive of a urea cycle disorder. Increased citrulline indicates a deficiency in either argininosuccinate synthase or argininosuccinate lyase (1). An increased plasma argininosuccinate concentration could differentiate these deficiencies, but that did not appear in the amino acid profile. The increased concentrations of leucine, homocysteine, and γ-aminobutyric acid are likely to be false increases caused by anhydrides of argininosuccinate coeluting with those molecules (2). Such interference would not be expected with liquid chromatography–mass spectrometry methods for newborn screening. The laboratory results in this case suggest argininosuccinate lyase deficiency.

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**References**


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**News & Views**

**Bring on the Biomarkers—It’s Time for the “Big Science” Approach**

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In the past decade, more than 150 000 publications have documented thousands of newly discovered candidate biomarkers representing hundreds of millions of dollars in research investment, yet only about 100 biomarkers have demonstrated potential clinical utility. Additionally, although large-scale and high-throughput technologies such as proteomics and genomics have held special promise for the discovery of novel biomarkers that can be used clinically, these promises have yet to be fulfilled. In a recent article in *Nature* (1), Dr. George Poste, the chief scientist at the Complex Adaptive Systems Initiative and Regents Professor of Health Innovation at Arizona State University, argues that “the dismal patchwork of fragmented research on disease-associated biomarkers should be replaced by a coordinated ‘big science’ approach.” Highlights of this article are summarized below.

Major components for the “big science” approach were suggested in the article. One is the standardization of sample, including procedures and documentation for sample collection and handling, sample storage, corresponding medical information, and identification of carefully matched samples from healthy individuals. In 2009, an NIH survey showed that about 80% of responding laboratories (>700 laboratories) indicated the difficulties in obtaining high-quality samples for their biomarker research. A strikingly high percentage of laboratories did not even consider sample quality. Consequently, many laboratories depend on whatever samples are conveniently available to conduct their biomarker research. Furthermore, the limited number of samples available at local institutions is usually insuffi-