

Hyperammonemia Clinical Presentation

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History

- Family history may reveal unexplained neonatal deaths or undiagnosed chronic illness. A history of males being affected is suggestive of OTC deficiency, which is inherited as an X-linked trait. Consanguinity results in an increased risk of inheriting a metabolic disorder.
- Early-onset hyperammonemia presents in the neonatal period. The baby is usually well for the first day or two. As the ammonia level rises, the baby becomes symptomatic. The family gives a history of lethargy, irritability, poor feeding, and vomiting. These symptoms correlate with an ammonia level of 100-150 $\mu\text{mol/L}$, which is 2-3 times the reference range. This may be followed by hyperventilation and grunting respiration; seizures also may develop.
- Late-onset hyperammonemia typically is due to urea cycle disorders, which can present later in life. The frequently altered clinical presentation of urea cycle disorders later in life develops from intrinsic differences in physiology based on age, as well as molecular aspects of the underlying biochemistry. Older children have greater energy reserves than neonates, allowing them to compensate for periods of stress. They also have a greater capacity and more opportunity to regulate their own environment. Adults with partial enzyme deficiency can become symptomatic when hyperammonemia is triggered by a stressful medical condition such as postpartum stress, heart-lung transplant, short bowel and kidney disease, parenteral nutrition with high nitrogen intake, and gastrointestinal bleeding.
 - Intermittent ataxia: Patients have an unstable gait and dysmetria. The intermittent nature of the symptoms is due to a periodic exacerbation of ammonia level.
 - Intellectual impairment: Episodic minor hyperammonemia may produce subtle intellectual deficits even in clinically asymptomatic individuals.
 - Failure to thrive: Children with an underlying metabolic disorder have suboptimal growth secondary to poor feeding and frequent vomiting.
 - Gait abnormality: In arginase deficiency, patients present with spastic diplegia, which manifests as toe walking.
 - Behavior disturbances: These include sleep disturbances, irritability, hyperactivity, manic episodes, and psychosis.
 - Epilepsy: Intractable seizures in a few patients have been secondary to an underlying urea cycle defect.
 - Recurrent Reye syndrome: A recurrent Reye syndromelike picture strongly suggests the possibility of a metabolic disorder.
 - Episodic headaches and cyclic vomiting may, rarely, be found to be caused by urea cycle defects.
 - Protein avoidance: Females with OTC deficiency may give a history of protein avoidance.

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