Research at a Glance

Researchers discover new gene variant for inherited amino acid-elevating disease

What's known:

Hypermethioninemia is a rare condition that causes elevated levels of methionine, an essential amino acid in humans. This condition stems from genetic variations inherited from one or both parents. Some forms of hypermethioninemia are recessive, meaning that two copies of defective genes are necessary to cause this disease. Other forms are dominant, meaning that only one copy can cause hypermethioninemia. Recessive forms of the disease tend to have more serious consequences, causing elevated methionine levels throughout life and leading to changes in the brain's white matter visible on magnetic resonance imaging that can cause neurological problems. The dominant forms are generally thought to be largely benign and require minimal follow-up.

What's new:

A research team led by Carlos R. Ferreira, M.D., a medical geneticist at Children's National Health System, discovered a new gene variant that had not been associated with hypermethioinemia previously when an infant who had tested positive for elevated methionine on newborn blood-spot screening came in for a follow-up evaluation. While the majority of dominant hypermethioninemia are caused by a genetic mutation known as *MAT1A* p.Arg264His, the child didn't have this or any of the common recessive hypermethioninemia mutations. Genetic testing showed that she carried a different mutation to the *MAT1A* gene known as p.Ala259Val, of which she carried only a single copy. The child fit the typical profile of having the dominant form of the disease, with methionine levels gradually declining over time. Testing of her mother showed that she carried the same gene variant, with few consequences other than a hepatitis-like illness as a child. Because liver disease can accompany dominant hypermethioninemia, the infant's doctors will continue periodic follow-up to ensure she remains healthy.

Questions for future research:

Q: Besides the potential for harmful liver effects, does dominant hypermethioninemia have other negative consequences?

Q: How common is this gene variant, and are certain people at more risk for carrying it?

Source: *"Confirmation that MAT1A p.Ala259Val mutation causes autosomal dominant hypermethioninemia." Muriello, M.J., S. Viall, T. Bottiglieri, K. Cusmano-Ozog and C. R. Ferreira. Published by Molecular Genetics and Metabolism Reports December 2017.*