MedicalXpress

Researchers identify genetic mutation causing lethal condition in infants

July 22 2015

Newborn children born with a mutation in the Plasmalemma Vesicle Associated Protein (PLVAP) gene develop severe protein losing enteropathy, according to a case study1 published in *Cellular and Molecular Gastroenterology and Hepatology*, the basic science journal of the American Gastroenterological Association. Protein losing enteropathy is a condition of the GI tract that results in loss of protein from the body, and often leads to severe abdominal swelling, malnutrition and early death in affected infants

The investigators utilized next-generation DNA sequencing to analyze an infant who died from severe protein losing enteropathy. The patient's symptoms largely resembled those of Plvap knockout mice at both ultrastructural and biochemical levels, strongly supporting a critical involvement of PLVAP in the development of protein losing enteropathy.

"These findings come at a critical time in medical research; the recent promise of gene therapy may make targeted correction of PLVAP mutations possible," said Dr. Abdul Elkadri, lead study author from the Hospital for Sick Children, Toronto, Ontario. "In the meantime, we can use these findings to develop more rapid diagnostic strategies to screen infants for this genetic mutation and prevent severe complications at an early stage of the disease."

Interestingly, in the case reported in *Cellular and Molecular Gastroenterology and Hepatology*, the defect caused by mutations in

PLVAP were due to increased leakage from small blood vessels rather than active loss from the cells lining the intestines. This finding is different from most cases of enteropathy, including the Microvillus Inclusion Disease and Congenital Tufting Enteropathy, which affect young children. In these latter conditions, genetic abnormalities cause cellular abnormalities primarily affecting intestinal epithelial tissue structure and function.

"As we move into the era of precision medicine, studies uncovering genetic causes of GI and liver disorders are much needed to guide the effective identification and treatment of patients," said James R. Goldenring, MD, PhD, AGAF, associate editor, *Cellular and Molecular Gastroenterology and Hepatology*. "A combination of basic research and clinical investigation, as exemplified by this work, will help achieve improved patient outcomes."

The study findings demonstrate two important concepts applicable to the broader medical community: first, mutations in single genes can lead to severe congenital abnormalities in newborn children, and second, mouse models are extremely useful in understanding congenital abnormalities in humans.

This novel monogenic lethal defect discovered by Dr. Elkadri and colleagues sheds fresh light on some new focus points, which must be explored by future studies.

More information: Elkadri, Abdul, et al. Mutations in Plasmalemma Vesicle Associated Protein (PLVAP) Result in Sieving Protein Losing Enteropathy Characterized by Hypoproteinemia, Hypoalbuminemia, and Hypertriglyceridemia, *Cellular and Molecular Gastroenterology and Hepatology* 2015: 1(4): 381-394.e7, www.cmghjournal.org/article/S2 … (15)00095-8/abstract

Provided by American Gastroenterological Association