Microvillus inclusion disease

Description

Microvillus inclusion disease is a condition characterized by chronic, watery, life-threatening diarrhea typically beginning in the first hours to days of life. Rarely, the diarrhea starts around age 3 or 4 months. Food intake increases the frequency of diarrhea.

Microvillus inclusion disease prevents the absorption of nutrients from food during digestion, resulting in malnutrition and dehydration. Affected infants often have difficulty gaining weight and growing at the expected rate (faltering weight), developmental delay, liver and kidney problems, and thinning of the bones (osteoporosis). Some affected individuals develop cholestasis, which is a reduced ability to produce and release a digestive fluid called bile. Cholestasis leads to irreversible liver disease (cirrhosis).

In individuals with microvillus inclusion disease, lifelong nutritional support is needed and given through intravenous feedings (parenteral nutrition).

A variant of microvillus inclusion disease with milder diarrhea often does not require full-time parenteral nutrition. Individuals with the variant type frequently live past childhood.

Frequency

The prevalence of microvillus inclusion disease is unknown. At least 200 cases have been reported in Europe, although this condition occurs worldwide.

Causes

Mutations in the *MYO5B* gene cause microvillus inclusion disease. The *MYO5B* gene provides instructions for making a protein called myosin Vb. This protein helps to determine the position of various components within cells (cell polarity). Myosin Vb also plays a role in moving components from the cell membrane to the interior of the cell for recycling.

MYO5B gene mutations that cause microvillus inclusion disease result in a decrease or absence of myosin Vb function. In cells that line the small intestine (enterocytes), a lack of myosin Vb function changes the cell polarity. As a result, enterocytes cannot properly form structures called microvilli, which normally project like small fingers from the surface of the cells and absorb nutrients and fluids from food as it passes through the

intestine. Inside affected enterocytes, small clumps of abnormal microvilli mix with misplaced digestive proteins to form microvillus inclusions, which contribute to the dysfunction of enterocytes. Disorganized enterocytes with poorly formed microvilli reduce the intestine's ability to take in nutrients. The inability to absorb nutrients and fluids during digestion leads to recurrent diarrhea, malnutrition, and dehydration in individuals with microvillus inclusion disease.

Some people with the signs and symptoms of microvillus inclusion disease do not have mutations in the *MYO5B* gene. These cases may be variants of microvillus inclusion disease. Studies suggest that mutations in other genes can cause these cases, but the causes are usually unknown.

Learn more about the gene associated with Microvillus inclusion disease

- MYO5B

Additional Information from NCBI Gene:

- STX3

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Congenital enteropathy
- Congenital familial protracted diarrhea with enterocyte brush-border abnormalities
- Congenital microvillous atrophy
- Davidson disease
- Familial protracted enteropathy
- Intractable diarrhea of infancy
- Microvillous atrophy
- Microvillous inclusion disease
- Microvillus atrophy with diarrhea 2
- MVID

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Congenital microvillous atrophy (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0341306/)

Genetic and Rare Diseases Information Center

- Microvillus inclusion disease (https://rarediseases.info.nih.gov/diseases/7039/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Microvillus inclusion disease%22)

Catalog of Genes and Diseases from OMIM

- DIARRHEA 2, WITH MICROVILLUS ATROPHY, WITH OR WITHOUT CHOLESTASIS; DIAR2 (https://omim.org/entry/251850)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28microvillus+inclusion+disease%5BTIAB%5D%29+OR+%28mvid%5BTIAB%5D%29+OR+%28congenital+microvillous+atrophy%5BTIAB%5D%29+OR+%28microvillous+atrophy%5BTIAB%5D%29+OR+%28microvillous+inclusion+disease%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

References

- Al-Daraji WI, Zelger B, Zelger B, Hussein MR. Microvillous inclusion disease:a clinicopathologic study of 17 cases from the UK. Ultrastruct Pathol. 2010Dec;34(6):327-32. doi: 10.3109/01913123.2010.500447. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21070163)
- Girard M, Lacaille F, Verkarre V, Mategot R, Feldmann G, Grodet A, Sauvat F,Irtan S, Davit-Spraul A, Jacquemin E, Ruemmele F, Rainteau D, Goulet O, Colomb V, Chardot C, Henrion-Caude A, Debray D. MYO5B and bile salt export pump contributeto cholestatic liver disorder in microvillous inclusion disease. Hepatology. 2014Jul;60(1):301-10. doi: 10.1002/hep.26974. Epub 2014 May 27. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24375397)

- Halac U, Lacaille F, Joly F, Hugot JP, Talbotec C, Colomb V, Ruemmele FM,Goulet O. Microvillous inclusion disease: how to improve the prognosis of asevere congenital enterocyte disorder. J Pediatr Gastroenterol Nutr. 2011Apr;52(4):460-5. doi: 10.1097/MPG.0b013e3181fb4559. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21407114)
- Khubchandani SR, Vohra P, Chitale AR, Sidana P. Microvillous inclusiondisease--an ultrastructural diagnosis: with a review of the literature.Ultrastruct Pathol. 2011 Apr;35(2):87-91. doi: 10.3109/01913123.2010.537438. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21299349)
- Knowles BC, Roland JT, Krishnan M, Tyska MJ, Lapierre LA, Dickman PS, Goldenring JR, Shub MD. Myosin Vb uncoupling from RAB8A and RAB11A elicitsmicrovillus inclusion disease. J Clin Invest. 2014 Jul;124(7):2947-62. doi:10.1172/JCI71651. Epub 2014 Jun 2. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24892806) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4071383/)
- Muller T, Hess MW, Schiefermeier N, Pfaller K, Ebner HL, Heinz-Erian P,Ponstingl H, Partsch J, Rollinghoff B, Kohler H, Berger T, Lenhartz H, SchlenckB, Houwen RJ, Taylor CJ, Zoller H, Lechner S, Goulet O, Utermann G, Ruemmele FM,Huber LA, Janecke AR. MYO5B mutations cause microvillus inclusion disease anddisrupt epithelial cell polarity. Nat Genet. 2008 Oct;40(10):1163-5. doi:10.1038/ng.225. Epub 2008 Aug 24. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18724368)
- Ruemmele FM, Muller T, Schiefermeier N, Ebner HL, Lechner S, Pfaller K, ThoniCE, Goulet O, Lacaille F, Schmitz J, Colomb V, Sauvat F, Revillon Y, Canioni D,Brousse N, de Saint-Basile G, Lefebvre J, Heinz-Erian P, Enninger A, Utermann G,Hess MW, Janecke AR, Huber LA. Loss-of-function of MYO5B is the main cause ofmicrovillus inclusion disease: 15 novel mutations and a CaCo-2 RNAi cell model.Hum Mutat. 2010 May;31(5):544-51. doi: 10.1002/humu.21224. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20186687)
- Thoeni CE, Vogel GF, Tancevski I, Geley S, Lechner S, Pfaller K, Hess MW,Muller T, Janecke AR, Avitzur Y, Muise A, Cutz E, Huber LA. Microvillus inclusiondisease: loss of Myosin vb disrupts intracellular traffic and cell polarity.Traffic. 2014 Jan;15(1):22-42. doi: 10.1111/tra.12131. Epub 2013 Nov 19. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24138727)
- Wiegerinck CL, Janecke AR, Schneeberger K, Vogel GF, van Haaften-Visser DY, Escher JC, Adam R, Thoni CE, Pfaller K, Jordan AJ, Weis CA, Nijman IJ, Monroe GR,van Hasselt PM, Cutz E, Klumperman J, Clevers H, Nieuwenhuis EE, Houwen RH, vanHaaften G, Hess MW, Huber LA, Stapelbroek JM, Muller T, Middendorp S. Loss ofsyntaxin 3 causes variant microvillus inclusion disease. Gastroenterology. 2014Jul;147(1):65-68.e10. doi: 10.1053/j.gastro.2014.04.002. Epub 2014 Apr 12. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24726755)

Last updated July 1, 2014