Autosomal recessive cerebellar ataxia type 1

Autosomal recessive cerebellar ataxia type 1 (ARCA1) is a condition characterized by progressive problems with movement due to a loss (atrophy) of nerve cells in the part of the brain that coordinates movement (the cerebellum). Signs and symptoms of the disorder first appear in early to mid-adulthood. People with this condition initially experience impaired speech (dysarthria), problems with coordination and balance (ataxia), or both. They may also have difficulty with movements that involve judging distance or scale (dysmetria). Other features of ARCA1 include abnormal eye movements (nystagmus) and problems following the movements of objects with the eyes. The movement problems are slowly progressive, often resulting in the need for a cane, walker, or wheelchair.

Frequency

More than 100 people have been diagnosed with ARCA1. This condition was first discovered in individuals from the Beauce and Bas-Saint-Laurent regions of Quebec, Canada, but it has since been found in populations worldwide.

Causes

Mutations in the *SYNE1* gene cause ARCA1. The *SYNE1* gene provides instructions for making a protein called Syne-1 that is found in many tissues, but it seems to be especially critical in the brain. Within the brain, the Syne-1 protein appears to play a role in the maintenance of the cerebellum, which is the part of the brain that coordinates movement. The Syne-1 protein is active (expressed) in Purkinje cells, which are located in the cerebellum and are involved in chemical signaling between nerve cells (neurons).

SYNE1 gene mutations that cause ARCA1 result in an abnormally short, dysfunctional version of the Syne-1 protein. The defective protein is thought to impair Purkinje cell function and disrupt signaling between neurons in the cerebellum. The loss of brain cells in the cerebellum causes the movement problems characteristic of ARCA1, but it is unclear how this cell loss is related to impaired Purkinje cell function.

Inheritance Pattern

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

- ARCA1
- autosomal recessive spinocerebellar ataxia 8
- recessive ataxia of Beauce

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Spinocerebellar ataxia, autosomal recessive 8
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1853116/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22autosomal+recessive+cerebellar+ataxia+type+1%22+OR+%22Cerebellar+Ataxia%22

Other Diagnosis and Management Resources

- GeneReview: SYNE1 Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1379
- Johns Hopkins Medicine Department of Neurology and Neurosurgery: What is Ataxia?
  https://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/ataxia/conditions/
- MedlinePlus Encyclopedia: Dysarthria--Care
  https://medlineplus.gov/ency/patientinstructions/000033.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Dysarthria--Care
  https://medlineplus.gov/ency/patientinstructions/000033.htm
- Encyclopedia: Movement--Uncoordinated
  https://medlineplus.gov/ency/article/003198.htm
- Health Topic: Balance Problems
  https://medlineplus.gov/balanceproblems.html

- Health Topic: Cerebellar Disorders
  https://medlineplus.gov/cerebellardisorders.html
- Health Topic: Movement Disorders
  https://medlineplus.gov/movementdisorders.html

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Ataxias and Cerebellar or Spinocerebellar Degeneration Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Ataxias-and-Cerebellar-or-Spinocerebellar-Degeneration-Information-Page

Educational Resources

- Johns Hopkins Medicine Department of Neurology and Neurosurgery: What is Ataxia?
  https://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/ataxia/conditions/
- Kennedy Krieger Institute: Movement Disorders
  https://www.kennedykrieger.org/patient-care/conditions/movement-disorders
- Orphanet: Autosomal recessive ataxia, Beauce type
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=88644
- Washington University, St. Louis: Neuromuscular Disease Center
  https://neuromuscular.wustl.edu/ataxia/recatax.html#ataxsyne1

Patient Support and Advocacy Resources

- Ataxia UK
  https://www.ataxia.org.uk/
- National Ataxia Foundation
  https://ataxia.org/

Clinical Information from GeneReviews

- SYNE1 Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1379

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SYNE1%5BTIAB%5D%29+AND+%28ataxia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- SPINOCEREBELLAR ATAXIA, AUTOSOMAL RECESSIVE 8
  http://omim.org/entry/610743

Sources for This Summary

- Dupré N, Gros-Louis F, Bouchard JP, Noreau A, Rouleau GA. SYNE1-Related Autosomal Recessive Cerebellar Ataxia. 2007 Feb 23 [updated 2011 Oct 13]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from http://www.ncbi.nlm.nih.gov/books/NBK1379/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301553
- Dupré N, Gros-Louis F, Chrestian N, Verreault S, Brunet D, de Verteuil D, Brais B, Bouchard JP, Rouleau GA. Clinical and genetic study of autosomal recessive cerebellar ataxia type 1. Ann Neurol. 2007 Jul;62(1):93-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17503513
- Gros-Louis F, Dupré N, Dion P, Fox MA, Laurent S, Verreault S, Sanes JR, Bouchard JP, Rouleau GA. Mutations in SYNE1 lead to a newly discovered form of autosomal recessive cerebellar ataxia. Nat Genet. 2007 Jan;39(1):80-5. Epub 2006 Dec 10.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17159980
- Izumi Y, Miyamoto R, Morino H, Yoshizawa A, Nishinaka K, Udaka F, Kameyama M, Maruyama H, Kawakami H. Cerebellar ataxia with SYNE1 mutation accompanying motor neuron disease. Neurology. 2013 Feb 5;80(6):600-1. doi: 10.1212/WNL.0b013e3182815529. Epub 2013 Jan 16. Erratum in: Neurology. 2013 Mar 26;80(13):1267.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23325900
- Noreau A, Bourassa CV, Szuto A, Levert A, Dobrzeniecka S, Gauthier J, Forlani S, Durr A, Anheim M, Stevanin G, Brice A, Bouchard JP, Dion PA, Dupré N, Rouleau GA. SYNE1 mutations in autosomal recessive cerebellar ataxia. JAMA Neurol. 2013 Oct;70(10):1296-31.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23959263

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