Muckle-Wells syndrome

Description

Muckle-Wells syndrome is a disorder characterized by periodic episodes of skin rash, fever, and joint pain. Progressive hearing loss and kidney damage also occur in this disorder.

People with Muckle-Wells syndrome have recurrent "flare-ups" that begin during infancy or early childhood. These episodes may appear to arise spontaneously or be triggered by cold, heat, fatigue, or other stresses. Affected individuals typically develop a non-itchy rash, mild to moderate fever, painful and swollen joints, and in some cases redness in the whites of the eyes (conjunctivitis).

Hearing loss caused by progressive nerve damage (sensorineural deafness) typically becomes apparent during the teenage years. Abnormal deposits of a protein called amyloid (amyloidosis) cause progressive kidney damage in about one-third of people with Muckle-Wells syndrome; these deposits may also damage other organs. In addition, pigmented skin lesions may occur in affected individuals.

Frequency

Muckle-Wells syndrome is a rare disorder. It has been reported in many regions of the world, but its prevalence is unknown.

Causes

Mutations in the *NLRP3* gene (also known as *CIAS1*) cause Muckle-Wells syndrome. The *NLRP3* gene provides instructions for making a protein called cryopyrin.

Cryopyrin belongs to a family of proteins called nucleotide-binding domain and leucine-rich repeat containing (NLR) proteins. These proteins are involved in the immune system, helping to regulate the process of inflammation. Inflammation occurs when the immune system sends signaling molecules and white blood cells to a site of injury or disease to fight microbial invaders and facilitate tissue repair. When this has been accomplished, the body stops (inhibits) the inflammatory response to prevent damage to its own cells and tissues.

Cryopyrin is involved in the assembly of a molecular complex called an inflammasome, which helps trigger the inflammatory process. Researchers believe that *NLRP3* gene

mutations that cause Muckle-Wells syndrome result in a hyperactive cryopyrin protein and an inappropriate inflammatory response. Impairment of the body's mechanisms for controlling inflammation results in the episodes of fever and damage to the body's cells and tissues seen in Muckle-Wells syndrome.

Learn more about the gene associated with Muckle-Wells syndrome

- NLRP3

Inheritance

This condition is usually inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In some cases, the inheritance pattern is unknown.

Other Names for This Condition

- Familial amyloid nephropathy with urticaria and deafness
- MWS
- UDA syndrome
- Urticaria-deafness-amyloidosis syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Familial amyloid nephropathy with urticaria AND deafness (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268390/)

Genetic and Rare Diseases Information Center

- Muckle-Wells syndrome (https://rarediseases.info.nih.gov/diseases/8472/muckle-wells-syndrome)

Patient Support and Advocacy Resources

- Disease InfoSearch (https://www.diseaseinfosearch.org/)
- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov (https://clinicaltrials.gov/ct2/results?cond=%22Muckle-Wells+syndrome%22)

Catalog of Genes and Diseases from OMIM

- MUCKLE-WELLS SYNDROME (https://omim.org/entry/191900)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28muckle-wells+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

References

- Aksentijevich I, Putnam CD, Remmers EF, Mueller JL, Le J, Kolodner RD, Moak Z, Chuang M, Austin F, Goldbach-Mansky R, Hoffman HM, Kastner DL. The clinicalcontinuum of cryopyrinopathies: novel CIAS1 mutations in North American patients and a new cryopyrin model. Arthritis Rheum. 2007 Apr;56(4):1273-1285. doi: 10.1002/art.22491. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17393462) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4321998/)
- Church LD, Cook GP, McDermott MF. Primer: inflammasomes and interleukin 1beta in inflammatory disorders. Nat Clin Pract Rheumatol. 2008 Jan;4(1):34-42. doi: 10.1038/ncprheum0681. Review. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18172447)
- Cuisset L, Drenth JP, Berthelot JM, Meyrier A, Vaudour G, Watts RA, Scott DG, Nicholls A, Pavek S, Vasseur C, Beckmann JS, Delpech M, Grateau G. Geneticlinkage of the Muckle-Wells syndrome to chromosome 1q44. Am J Hum Genet. 1999Oct;65(4):1054-9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10486324) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1288238/)
- Dodé C, Le Dû N, Cuisset L, Letourneur F, Berthelot JM, Vaudour G, Meyrier A, Watts RA, Scott DG, Nicholls A, Granel B, Frances C, Garcier F, Edery P, Boulinguez S, Domergues JP, Delpech M, Grateau G. New mutations of CIAS1 that areresponsible for Muckle-Wells syndrome and familial cold urticaria: a novelmutation underlies both syndromes. Am J Hum Genet. 2002 Jun;70(6):1498-506. Epub 2002 Apr 25. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11992256) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC379138/)
- El-Darouti MA, Marzouk SA, Abdel-Halim MR. Muckle-Wells syndrome: report ofsix cases with hyperpigmented sclerodermoid skin lesions. Int J Dermatol. 2006Mar;45(3):239-44. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16533222)
- Farasat S, Aksentijevich I, Toro JR. Autoinflammatory diseases: clinical andgenetic advances. Arch Dermatol. 2008 Mar;144(3):392-402. Review. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18347298)

- Gerbig AW, Dahinden CA, Mullis P, Hunziker T. Circadian elevation of IL-6levels in Muckle-Wells syndrome: a disorder of the neuro-immune axis? QJM. 1998Jul;91(7): 489-92. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/9797932)
- Haas N, Küster W, Zuberbier T, Henz BM. Muckle-Wells syndrome: clinical andhistological skin findings compatible with cold air urticaria in a large kindred.Br J Dermatol. 2004 Jul;151(1):99-104. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15270877)
- Hawkins PN, Lachmann HJ, McDermott MF. Interleukin-1-receptor antagonist inthe Muckle-Wells syndrome. N Engl J Med. 2003 Jun 19;348(25):2583-4. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12815153)
- Hoffman HM, Mueller JL, Broide DH, Wanderer AA, Kolodner RD. Mutation of a newgene encoding a putative pyrin-like protein causes familial cold autoinflammatorysyndrome and Muckle-Wells syndrome. Nat Genet. 2001 Nov;29(3): 301-5. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11687797) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4322000/)
- Kanazawa N, Furukawa F. Autoinflammatory syndromes with a dermatologicalperspective. J Dermatol. 2007 Sep;34(9):601-18. Review. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17727363)
- Stankovic K, Grateau G. Auto inflammatory syndromes: Diagnosis and treatment. Joint Bone Spine. 2007 Dec;74(6):544-50. Epub 2007 Sep 20. Review. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17950649)
- Tunca M, Ozdogan H. Molecular and genetic characteristics of hereditaryautoinflammatory diseases. Curr Drug Targets Inflamm Allergy. 2005Feb;4(1):77-80. Review. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15720239)
- Watts RA, Nicholls A, Scott DG. The arthropathy of the Muckle-Wells syndrome. Br J Rheumatol. 1994 Dec;33(12):1184-7. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/8000753)

Page last updated on 18 August 2020

Page last reviewed: 1 September 2008