Dent disease

Description

Dent disease is a chronic kidney disorder that occurs almost exclusively in males. In affected individuals, kidney problems result from damage to structures called proximal tubules. Signs and symptoms of this condition appear in early childhood and worsen over time.

The most frequent sign of Dent disease is the presence of an abnormally large amount of proteins in the urine (tubular proteinuria). Other common signs of the disorder include excess calcium in the urine (hypercalciuria), calcium deposits in the kidneys (nephrocalcinosis), and kidney stones (nephrolithiasis). Kidney stones can cause abdominal pain and blood in the urine (hematuria). In most affected males, progressive kidney problems lead to end-stage renal disease (ESRD) in early to mid-adulthood. ESRD is a life-threatening failure of kidney function that occurs when the kidneys are no longer able to filter fluids and waste products from the body effectively.

Some people with Dent disease develop rickets, a bone disorder that results when the levels of vitamin D and certain minerals (including calcium) in the blood become too low. Rickets can be associated with weakening and softening of the bones, bone pain, bowed legs, and difficulty walking.

Researchers have described two forms of Dent disease, which are distinguished by their genetic cause and pattern of signs and symptoms. Both forms of Dent disease (type 1 and type 2) are characterized by the features described above, but Dent disease 2 can also be associated with abnormalities unrelated to kidney function. These additional signs and symptoms include mild intellectual disability, weak muscle tone (hypotonia), and clouding of the lens of the eyes (cataract) that is described as subclinical because it does not impair vision. Some researchers consider Dent disease 2 to be a mild variant of a similar disorder called Lowe syndrome.

Frequency

Dent disease is a rare condition, with about 250 affected families reported. Dent disease 1 is more common than Dent disease 2.

Dent disease is likely underdiagnosed because it may not be identified in people with mild signs and symptoms, and because its features overlap with those of other kidney disorders.

Causes

Dent disease can result from mutations in the *CLCN5* or *OCRL* gene. Mutations in the *CLCN5* gene cause Dent disease 1, which accounts for about 60 percent of all cases of Dent disease. Mutations in the *OCRL* gene cause Dent disease 2, which accounts for about 15 percent of all cases. In the remaining 25 percent of cases, the genetic cause of the disorder is unknown.

The proteins produced from the *CLCN5* and *OCRL* genes play critical roles in normal kidney function, particularly the function of the proximal tubules. These structures help to reabsorb nutrients, water, and other materials that have been filtered from the bloodstream. The kidneys reabsorb needed materials into the blood and excrete everything else into the urine. Studies suggest that mutations in the *CLCN5* or *OCRL* gene disrupt the reabsorption function of the proximal tubules, which leads to the progressive kidney problems found in people with Dent disease.

Because the *OCRL* gene is active (expressed) throughout the body, it is unclear why Dent disease 2 primarily affects the kidneys and, to a lesser extent, the brain, eyes, and other tissues.

Learn more about the genes associated with Dent disease

- CLCN5
- OCRL

Inheritance

Dent disease is inherited in an X-linked recessive pattern. The *CLCN5* and *OCRL* genes are located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of a gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In X-linked recessive inheritance, a female with one mutated copy of the gene in each cell is called a carrier. She can pass on the altered gene but usually does not experience signs and symptoms of the disorder. However, some females who carry a mutation in the *CLCN5* or *OCRL* gene have mild features of Dent disease, including proteinuria and hypercalciuria. Severe kidney problems, including ESRD, are rare in female carriers.

Other Names for This Condition

- Dent's disease
- Dents disease

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Dent disease type 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848336/)
- Genetic Testing Registry: Dent disease type 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1845167/)

Genetic and Rare Diseases Information Center

- Dent disease (https://rarediseases.info.nih.gov/diseases/13105/index)

Patient Support and Advocacy Resources

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

Clinical Trials

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

Catalog of Genes and Diseases from OMIM

- DENT DISEASE 1; DENT1 (https://omim.org/entry/300009)
- DENT DISEASE 2; DENT2 (https://omim.org/entry/300555)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28Dent+disease%5BMH%5D%29+OR+%28Dent+disease%5BTI%5D%29+OR+%28Dent's+disease%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

References

- Claverie-Martin F, Ramos-Trujillo E, Garcia-Nieto V. Dent's disease: clinicalfeatures and molecular basis. Pediatr Nephrol. 2011 May;26(5):693-704. doi: 10.1007/s00467-010-1657-0. Epub 2010 Oct 10. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20936522)
- Devuyst O, Thakker RV. Dent's disease. Orphanet J Rare Dis. 2010 Oct 14;5:28.doi: 10.1186/1750-1172-5-28. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20946626) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2964617/)

- Devuyst O. Dent's disease: chloride-proton exchange controls proximal tubuleendocytosis. Nephrol Dial Transplant. 2010 Dec;25(12):3832-5. doi:10.1093/ndt/gfq556. Epub 2010 Sep 6. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20819956)
- Hichri H, Rendu J, Monnier N, Coutton C, Dorseuil O, Poussou RV, Baujat G, Blanchard A, Nobili F, Ranchin B, Remesy M, Salomon R, Satre V, Lunardi J. FromLowe syndrome to Dent disease: correlations between mutations of the OCRL1 geneand clinical and biochemical phenotypes. Hum Mutat. 2011 Apr;32(4):379-88. doi:10.1002/humu.21391. Epub 2011 Mar 10. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21031565)
- Hoopes RR Jr, Shrimpton AE, Knohl SJ, Hueber P, Hoppe B, Matyus J, Simckes A, Tasic V, Toenshoff B, Suchy SF, Nussbaum RL, Scheinman SJ. Dent Disease withmutations in OCRL1. Am J Hum Genet. 2005 Feb;76(2):260-7. doi: 10.1086/427887.Epub 2004 Dec 30. Erratum In: Am J Hum Genet. 2007 Sep;81(3):634. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15627218) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1196371/)
- Lloyd SE, Gunther W, Pearce SH, Thomson A, Bianchi ML, Bosio M, Craig IW, Fisher SE, Scheinman SJ, Wrong O, Jentsch TJ, Thakker RV. Characterisation ofrenal chloride channel, CLCN5, mutations in hypercalciuric nephrolithiasis(kidney stones) disorders. Hum Mol Genet. 1997 Aug;6(8):1233-9. doi:10.1093/hmg/6.8.1233. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/9259268)
- Ludwig M, Utsch B, Monnens LA. Recent advances in understanding the clinicaland genetic heterogeneity of Dent's disease. Nephrol Dial Transplant. 2006Oct;21(10):2708-17. doi: 10.1093/ndt/gfl346. Epub 2006 Jul 20. No abstractavailable. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16861240)
- Wrong OM, Norden AG, Feest TG. Dent's disease; a familial proximal renaltubular syndrome with low-molecular-weight proteinuria, hypercalciuria, nephrocalcinosis, metabolic bone disease, progressive renal failure and a markedmale predominance. QJM. 1994 Aug;87(8):473-93. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/7922301)

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