Dent disease

Description

Dent disease is a chronic kidney disorder that occurs almost exclusively in males. The kidney problems seen in affected individuals are a result of damage to structures called proximal tubules. These structures help reabsorb water, protein, and other nutrients into the bloodstream or release them into the urine.

The signs and symptoms of Dent disease tend to appear in childhood and worsen over time. However, the features and the severity of Dent disease vary greatly among affected individuals.

The most frequent sign of Dent disease is the loss of small proteins in the urine (also called low-molecular-weight or LMW proteinuria). Too much calcium in the urine (hypercalciuria) is another common sign of Dent disease. LMW proteinuria and hypercalciuria may be the only signs of Dent disease in affected children.

Additional signs and symptoms of Dent disease can include calcium deposits in the kidneys (nephrocalcinosis) and kidney stones (nephrolithiasis). Kidney stones can cause abdominal pain and blood in the urine (hematuria). Thirty to 80 percent of people with Dent disease develop kidney failure in early to mid-adulthood. Kidney failure can be life-threatening and occurs when the kidneys are no longer able to effectively filter fluids and waste products from the body.

In some people with Dent disease, low levels of vitamin D and other factors can cause bones to soften and weaken. This can result in a condition called rickets or a similar condition called osteomalacia. These conditions can cause bone pain and make bones more likely to break. Rickets can also be associated with bowed legs, difficulty walking, and short stature.

Researchers have described two forms of Dent disease that are caused by changes in different genes: Dent disease 1 and Dent disease 2. Both forms are characterized by the features described above, but Dent disease 2 can also be associated with mild intellectual disabilities and developmental delays. People with Dent disease 2 may also have a clouding of the lens of the eye (cataract) that does not typically cause severe visual impairment. Studies have also suggested that people with Dent disease 2 may be more likely to develop a painful skin condition called hidradenitis suppurativa.

Frequency

Approximately 850 families with Dent disease have been reported in the scientific literature. However, because the features of Dent disease can vary and may overlap with those seen in other disorders, this number may not accurately represent the number of people with this condition.

Causes

Changes in the *CLCN5* gene cause Dent disease 1, while changes in the *OCRL* gene cause Dent disease 2. Genetic changes that cause disease are called pathogenic variants. Approximately 60 percent of people with Dent disease have type 1. Another 15 to 20 percent of people with Dent disease have type 2.

The proteins produced from the *CLCN5* and *OCRL* genes play important roles in normal kidney function, particularly within the proximal tubules. Studies suggest that certain pathogenic variants in the *CLCN5* or *OCRL* genes lead to abnormal protein reabsorption within the proximal tubules. As a result, proteins that should be reabsorbed into the bloodstream are released in the urine. This leads to the kidney problems seen in people with Dent disease.

Approximately 20 to 25 percent of people with Dent disease do not have an identified variant in the *CLCN5* or *OCRL* genes. The cause of the condition in these cases is not known.

Learn more about the genes associated with Dent disease

- CLCN5
- OCRL

Inheritance

Dent disease is inherited in an X-linked pattern. The *CLCN5* and *OCRL* genes are located on the X chromosome, which is one of the two sex chromosomes in each cell. In males (who have only one X chromosome), a pathogenic variant in the only copy of the gene in each cell is typically sufficient to cause the condition. This is not always the case for X-linked disorders in females (who have two X chromosomes in each cell). However, some females with a pathogenic variant in the *CLCN5* or *OCRL* gene have mild features of Dent disease, including LMW proteinuria, hypercalciuria, and nephrolithiasis. Kidney failure in females is extremely rare. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Some cases of Dent disease likely result from a new (de novo) variant in the gene that occurs during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or during early embryonic development. These affected individuals typically have no history of the disorder in their family.

Other Names for This Condition

- Dent syndrome
- Dent's disease
- Dents disease
- Low-molecular-weight proteinuria with hypercalciuria and nephrocalcinosis
- Renal Fanconi syndrome with nephrocalcinosis and renal stones
- X-linked recessive hypercalciuric hypophosphatemic rickets
- X-linked recessive nephrolithiasis

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

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